The timing of learned eyelid responses depends on causality in the cerebellar-red-nucleus-motoneuron network

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Abstract

Although data collected from different types of experiments indicate that wide brain areas – including cerebral and cerebellar cortices, as well as basal ganglia – are involved in different aspects of timing and time perception, the information on the actual neural mechanisms supporting those timed behaviors is rather scarce. In particular, the cerebellar-interpositus/red-nucleus-motoneuron network has been reported as being involved in the dynamic control and timing of the eyelid kinematics. Here we present a meta-analysis revealing how the involved neural structures can change their activities during eyeblink conditioning. In this work, the close relation between the timing of learned responses and the causality in the network was verified.

Keywords: Timing; Causality; Kinematics; Associative learning; Eyeblink conditioning; Cerebellum; Interpositus nucleus

1. Introduction

The generation of eyelid conditioned responses (CRs) is a slow process requiring a large number of paired conditioned stimulus (CS) / unconditioned stimulus (US) presentations, as we have already described for mice, rats, rabbits, and cats (Domínguez-del-Toro et al., 2004; Gruart et al., 1995, 2000, 2006; Pacheco-Calderón et al., 2012; Porras-García et al, 2010; Sánchez-Campusano et al., 2007; Trigo et al., 1999; Valenzuela-Harrington et al., 2007).

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This associative learning process involves different temporal domains of measurement (Buhusi & Meck, 2005) for multiple parameters, including milliseconds timing (intra-trial events), the temporal range of definition of interval timing (seconds-to-minutes-to-hours, inter-trial and inter-block interactions), and the temporal evolution across a proper sequence of training days or successive conditioning sessions (inter-session interactions). This variability in temporal domains of the learning process makes it implausible that the neuronal mechanisms involved are dependent on fixed time constants as, for example, has been proposed in models of timed behavior in the context of classical conditioning (Fiala et al., 1996; Grossberg & Schmajuk 1989). Furthermore it has been shown that a central spatiotemporal coding (firing rate code and spike timing), more than the timing or firing rate codes separately, can support the cerebellar processing (De Zeeuw et al., 2011). This strategy of spatiotemporal patterns expanded the functional domain of cerebellar timing beyond motor control and shows the need for a time-intensity code of the kinetic neural commands and the kinematic parameters collected during the associative learning process. Thus, timed behavior (Buonomano & Karmarkar, 2002; Buonomano & Laje, 2010; Clarke et al., 1996; Mauk & Buonomano 2004; Medina et al., 2005; Svensson et al., 2010) could be distinguished from other types of timing strategies, such as, for example, the interval timing. Interval timing is usually defined as the ability to modify a behavioral response as a function of the arbitrary duration (seconds to hours) of a given time interval (Buhusi & Meck, 2005; Gallistel & Gibbon, 2000; Lewis, 2003; Staddon & Higa, 1999; Staddon & Cerutti, 2003). Thus, in experimental studies of interval timing, subjects are presented with time intervals of different durations, with the main aim being to determine how the temporal distribution of responses changes as a function of interval duration. Results obtained in these types of study indicate that, in many occasions, they are time-scale invariant (Gibbon, 1977; Lejeune & Wearden, 2006; Wearden & Lejeune, 2008) and that the temporal distributions of responses for two different interval durations are the same if the time-axis is divided by the duration of the interval (Almeida & Ledberg, 2010). Available data reveal a wide range of interval durations over which time-scale invariance has been demonstrated. Indeed, in some tasks this range covers two orders of magnitude (Gibbon 1977; Gibbon & Church, 1990; Gibbon et al., 1997). In this sense, some authors have developed a model of an interval timing device of bistable units with random state that is consistent with time-scale invariant behavior over a substantial time-range (Almeida & Ledberg, 2010; Miall, 1993; Okamoto & Fukai, 2001; Okamoto et al., 2007). The idea of working with different durations of the inter-stimulus interval and to study the different temporal distributions of the response is also included in studying timed behaviors. However, the information on the actual neural mechanisms supporting those timed behaviors should be interpreted as a result of the analysis of the dynamic/plastic changes that occur at the different time domains (i.e., from sub-second range (millisecond timing) to longer-lasting ranges]).

In particular, the cerebellar-interpositus/red-nucleus-motoneuron pathway has been repeatedly reported as being involved in the generation, control, and expression of conditioned eyelink (Bracha et al., 2001; Christian & Thompson, 2003; Krupa et al., 1993; Mauk, 1997; Woody, 1986), or at least in the proper performance of reflex and acquired eyelid responses (Bracha et al., 2009; Delgado-Garcia & Gruart, 2002, 2006; Gruart et al., 2000; Sánchez-Campusano et al., 2007, 2009; Welsh & Harvey, 1991; Welsh, 1992). Moreover, it has been proposed that this pathway is involved in the adequate timing of classically conditioned eyelid responses (Boele et al., 2009; García & Mauk, 1998; Koekkoe et al., 2003, 2005; Sánchez-Campusano et al., 2011a,b, 2012). However, there is not a single study attempting to integrate the kinetic neural commands emanating from those neuronal centers, the eyelid kinematics and the correlation code between them, as well as the causal inferences in the involved neural network, in order to obtain a complete and clear picture of events taking place simultaneously at the different functional states during the acquisition of this type of learned motor response. The results presented here are based mostly on data collected from experiments carried out elsewhere (Gruart et al., 2000; Delgado-Garcia & Gruart, 2002; Trigo et al., 1999). Our aim here was to re-analyze in detail selected kinetic neural commands of interpositus nucleus (IP) neurons and orbicularis oculi (OO) motoneuron (MN), as well as the OO electromyography (EMG) activity and eyelid kinematic collected during delay eyelink conditioning. Thus, we decided to investigate the relations between timing of learned eyelid responses and the causality in the cerebellar-interpositus/red-nucleus-motoneuron network, using a coherent mixture of simple circular statistics (timing-intensity dispersion patterns), directional analysis (time delays and correlation code), and causality (time-dependent causal inferences) for the data acquired during the conditioning process. We believe that this analytical-experimental approach could be useful for a better understanding of events taking place at different brain sites (not only the ones analyzed here) and of the motor responses acquired during this simple model of associative learning task.
2. Results

2.1. Timing and time-intensity dispersion patterns of types A and B IP neurons and OO MNs during motor learning

We selected as the timing components of the circular distributions (Fig. 1a) the time to peak firing rate of the type A IP neurons (see cyan arrows), the time to CR onset (brown arrows) and the time delay between eyelid position and type A IP neurons firing rate (red arrows). The intensity components of the distributions were the peak-firing rate of type A IP neurons, the percentage of CRs and the linear correlation coefficient, respectively. Here, the timing–intensity associations enabled us to illustrate the simultaneous evolution of the timing and intensity components of the data distributions (from OO MNs and type A IP neuron firing activities, and eyelid CRs). Note the inverse interrelations between the percentage of CRs and the time to CRs onset (brown arrows), and between the peak firing rate of type A IP neurons and their corresponding time of occurrence (cyan arrows) across this associative learning test. The circumferences and the circular sectors in Fig. 1 show the relative dispersion patterns of the time-intensity distributions. For example, in Fig. 1a the mean values of the time to peak firing rate of type A IP neurons across the conditioning sessions [cyan arrows, \( \rho_s = 10.92 \pm 1.01 \), \((\text{mean} \pm \text{SEM})\)] were less spread out than the mean values of either time to CRs onset [brown arrows, \( \rho_s = 14.94 \pm 1.23 \), \((\text{mean} \pm \text{SEM})\)] or time delay in coupling between type A IP neurons firing frequency and eyelid position response [red arrows, \( \rho_s = 45.84 \pm 2.48 \), \((\text{mean} \pm \text{SEM})\)].

These time-intensity patterns allowed us to verify the previous results, – i.e., the time to peak firing rate of type A IP neurons always lagged the beginning of the CRs [blue arrows, mean timing \( \bar{T}_s = 67.64 \pm 3.07 \text{ ms}, (\text{mean} \pm \text{SEM}); \text{brown arrows, mean timing } \bar{T}_s = 52.62 \pm 1.89 \text{ ms}, (\text{mean} \pm \text{SEM})\)]. Interestingly, the dispersion of the time delay of the correlation (type A IP neurons vs. eyelid position) showed a significantly [one-way ANOVA F-tests, \( F(9, 27, 98) = 223.54, P < 0.01 \)] longer transition from larger to smaller values, than did the time to peak firing rate of type A IP neurons across the sessions. Thus, to the beginning of the learning process the type A IP neurons encoded (from moderate to weak correlation) eyelid position responses after reaching their maximum firing rate, but at the end of the process (i.e., at the asymptotic level of acquisition of this associative learning test) the IP neurons encoded (with barely significant correlation) eyelid kinematics before their peak firing rate (but always after the beginning of the CRs).

In geometric terms, the centroid of the blue circular sector (corresponding to the time to peak firing rate of the type A IP neurons in Fig. 1a) was much further away from the center of the circumference than the centroid of the red circular sector [corresponding to time delay of the correlation (type A IP neurons vs. eyelid position)] was from the center of the same circumference – that is, the index of circular spread of the blue circular sector \( [\sigma = 5.77 \pm 0.56; \bar{T} = 69.74 \pm 2.26 \text{ ms}, (\text{mean} \pm \text{SEM})] \) was smaller than the time-dispersion index of the red circular sector \( [\sigma = 32.71 \pm 1.16, \bar{T} = 77.48 \pm 3.05 \text{ ms}, (\text{mean} \pm \text{SEM})] \). This is generally the case - data sets with a greater degree of dispersion have centroids closer to the center of the circumference.

In the same way, in Fig. 1b we illustrate the time-intensity distributions for the type B IP neurons (see the gray and orange arrows). Here, we selected as the intensity components of the distributions the peak-firing rate of type B IP neurons in the modulation range of the pause, and the lowest firing frequency of type B IP neurons during the pause. The timing components of the distributions were the time to peak firing rate of type B IP neurons in the modulation range of the pause, and the time to lowest firing frequency of type B IP neurons during the pause with respect to CS presentation. The time-intensity components of the neuronal distribution allowed us to determine the relative time dispersion patterns between type B neural commands and the eyelid kinematics (see the gray and brown circular sectors in Fig. 1b). According to data shown in Fig. 1b, the time to lowest firing rate of type B IP neurons always lagged the beginning of the CRs [gray arrows, mean timing \( \bar{T}_s = 70.11 \pm 2.80 \text{ ms}, \text{green circular sector, mean timing } \bar{T} = 71.26 \pm 3.03 \text{ ms}, (\text{mean} \pm \text{SEM}); \text{brown arrows, mean timing } \bar{T}_s = 52.62 \pm 1.89 \text{ ms}, \text{brown circular sector, } \bar{T} = 56.92 \pm 2.17 \text{ ms}, (\text{mean} \pm \text{SEM})\)].

In Fig. 1c, the time delay–strength distributions were conformed using the time delays in coupling between the physiological signals (\( \tau_1 \) and \( \tau_2 \), see magenta arrows; \( \tau_3 \) and \( \tau_4 \), see blue arrows; \( \tau_5 \) and \( \tau_6 \), see green arrows) and their corresponding correlation code parameters. A summary of the direction and causality indices is shown in Table 1.
Fig. 1. The time-intensity and time delay-strength distributions of the data collected across 10 conditioning sessions. (a, b) Timing of the eyelid CRs (brown arrows) in relation to the timing of the kinetic neural commands of type A [cyan arrows in (a)] and type B [gray arrows in (b)] cerebellar posterior IP neurons. The colored circular sectors illustrate the time-dispersion range of the data collected during eyeblink conditioning, including the time-strength pattern (red arrows) of the linear correlation between the IP neurons firing rate and eyelid position. In (b), the gray arrows represent the dispersion pattern for the time to lowest firing rate of type B IP neurons and the pink arrows indicate the time to peak firing rate of type B IP neurons in the modulation range of the pause. Here, the yellow circular sector indicates the temporal range of the beginning of the pause, and the orange circular arrow represents the duration of the pause (including the temporal ranges for the yellow and gray circular sectors). (c) The time delay-strength dispersion patterns of type A IP neurons for all the dynamic associations. Notice the close relation between direction and causal inferences. Nine circular distributions (different sets of color arrows and circular sectors) represent the time-intensity dispersion patterns across conditioning sessions (C01–C10). [This figure was taken, modified and reproduced with permission from Sánchez-Campusano et al. (2011b)].

Table 1. Summary of the direction and causality analyses for the three main dynamic associations, according to: the asymmetry information ($\Delta \eta$), the time delays ($\Delta \tau$) of coupling between the electrophysiological recordings, the direction index ($D$), and the normal ($G_{1,0}$) and standardized ($K_{G1,0}$) Granger causality indices.

<table>
<thead>
<tr>
<th>Association</th>
<th>Direction information</th>
<th>Causality inferences</th>
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<tbody>
<tr>
<td>Dynamic association (MN</td>
<td>EMG)</td>
<td>$\Delta \eta_{12_{max}} &gt; 0; \Delta \tau_{12} &gt; 0; D_{12} = 1$</td>
</tr>
<tr>
<td>Dynamic association (IP</td>
<td>EMG)</td>
<td>$\Delta \eta_{34_{max}} &gt; 0; \Delta \tau_{34} &gt; 0; D_{34} = 0$</td>
</tr>
<tr>
<td>Dynamic association (IP</td>
<td>MN)</td>
<td>$\Delta \eta_{56_{max}} &gt; 0; \Delta \tau_{56} &gt; 0; D_{56} = 0$</td>
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For the dynamic associations between IP neurons and either OO MNs or OO EMG recordings the relationships between the time delay and strength components of the distributions were direct but diminishing across the conditioning sessions (see the blue and green arrows in Fig. 1c).

In contrast, for the coupling between MNs and OO EMG recordings, the relationships between time delay and strength components were inverse – that is, while the nonlinear association indices were increasing, their corresponding time delays $F(9, 27, 98) = 66.29, P < 0.01$; and $F(9, 27, 98) = 49.16, P < 0.01$ were decreasing across conditioning sessions in the opposed sense to the hands of the clock (i.e., from US to CS, see the black circular arrows in the circular sectors of the Fig. 1c).

According to the circular representations in Fig. 1c, the time-dispersion indices of the green circular sectors [for time delay components $F(9, 27, 98) = 121.78, P < 0.01$; and $F(9, 27, 98) = 188.40, P < 0.01$, respectively] were larger than the indices of circular spread of the blue circular sectors [for time delay components $F(9, 27, 98) = 119.36, P < 0.01$; and $F(9, 27, 98) = 171.05, P < 0.01$, respectively]. Furthermore, the time delays between the cerebellar IP neuron raw recording and the OO EMG activity in the two directions of coupling (see the blue sectors in Fig. 1c) always lagged the start of the CRs (see the brown circular sector).

As a summary, whereas OO MNs encoded eyelid kinematics and generated the natural oscillatory properties of the neuromuscular elements involved in the eyeblinks, interpositus neurons did not directly encode eyelid performance, and the timing/time-delays of its kinetic neural commands were not consistent with the timing of the learned eyelid responses.

2.2. Design of an experimental-analytical tool to analyze the timing of CRs and the causality of the network

The nonlinear dynamic associations and time-dependent Granger causality of physiological time series, the circular statistics of the dataset distributions, and the hierarchical cluster technique are optimal analytical tools for studying the interactions among timing parameters, kinematic variables, correlation codes, time delay information, dispersion patterns, and finally, the directionality/causality indices (see Fig. 2a) conforming the forty-dimension vectors of learning states during motor learning.

The results used here enable us to determine the intrinsic coherence (Fig. 2b) of collected data and the relationship between timing and causality in the cerebellar-interpositus/red nucleus-motoneuron network in different temporal domains (in the range of milliseconds for intra-trials interactions; in the range of seconds, minutes, and hours for both inter-trials and inter-blocks interactions; and in the range of days for the inter-blocks interactions along the process). For this, we have developed the necessary computer programs and algorithmic procedures to deal with such a huge amount of data (40 parameters quantified across 180 averaged blocks and 15 experimental sessions collected from 8 experimental animals).

The computer program arranged the data in a total of 180 blocks (15 conditioning sessions × 12 blocks) according to their significant homogeneity: namely, blocks within clusters were displayed close together when plotted geometrically according to linkage distances, whereas different clusters were displayed far apart.

The main result according to the actual causality inferences (see the left-hand hierarchical cluster trees in Fig. 2b) indicated that up to 147 blocks could be correctly assigned to the corresponding experimental (habituation, conditioning, or extinction) session, and only data collected from 33 blocks were discarded because of their low homogeneity with the corresponding session.

Here, the threshold linkage distance was of only 46.57 units (see green dashed line) and the hierarchical cluster trees were significantly consistent (high cophenetic correlation coefficient, 0.9802; the closer this value is to 1, the better the clustering) with the actual conditioning sessions.

According to the left-hand dendrogram D1 (see Fig. 2a, for the actual causality), the 15 significant clusters corresponded to 147 averaged blocks distributed in the 15 experimental sessions during the delay conditioning paradigm (H01-H02 = 19, C01-C10 = 108, and E01-E03 = 20 blocks). Here, notice a coherent nodal distribution (see the vertical colored bars in the left-hand panel) in correspondence with a proper trend in the evolution of the conditioning process.
Fig. 2. (a) The diagram illustrates the definition of a forty-dimension state vector of parameters (1–40) formed by 5 timing parameters (from 1 to 5), 4 kinetic neural commands (from 6 to 9), 2 kinematic variables (10 and 11), 7 correlation code parameters (from 12 to 18), 7 time delays (from 19 to 25), 9 dispersion patterns (from 26 to 34), and finally 6 direction and causality indices (from 35 to 40). (b) Hierarchical cluster trees of averaged blocks using the forty-dimension vectors of learning states collected across habituation (H01-H02), conditioning (C01-C10), and extinction (E01-E03) sessions. The dendrograms illustrate the hierarchical distributions of the averaged blocks of conditioning in accordance with both actual (the left-hand dendrogram, D1) and simulated (the right-hand dendrogram, D2) causality inferences. Each color bar at the bottom represents an averaged conditioning block. The linkage-weighted distances are represented on the x-axes. The comparison depth was of 16 levels. The y-axes represent, as colored (not black) lines, the statistically significant clusters [D1, 15 significant clusters, 147 averaged blocks, $F(14, 70, 132) = 36.1213, P < 0.01$, Wilk’s lambda = 0.09, with $N_R = 5$; D2, 10 significant clusters, 166 averaged blocks, $F(9, 45, 156) = 2.4290, P < 0.05$, Wilk’s lambda = 0.26, with $N_R = 5$]. The black lines represent the averaged blocks that fall into the remaining statistically non-significant clusters. In the dendrogram D1, notice a coherent nodal distribution (see the vertical colored bars in the left-hand panel) in correspondence with a proper trend in the evolution of the conditioning process. However, for dendrogram D2 (simulated causality inferences), the total number of significant clusters was of 10 groups – i.e., an insufficient number of groups to match with the 15 conditioning sessions. [This figure was taken and reproduced with permission from Sánchez-Campusano et al. (2011b)].
However, for the simulated causality conditions (see the right-hand hierarchical cluster trees in Fig. 2b), where only the directionality and causality indices (see Table 1) that involved the IP neurons interdependencies were modified randomly (sequence of 0 or 1 for the parameters 36, 37, 39, and 40 of each averaged block, in Fig. 5a) prior to application of the clustering algorithm, the clusters were obtained with evident linkage alterations and inconsistency (moderate cophenetic correlation coefficient, 0.6836) affecting the typical and sequential temporal distribution of training blocks (see the yellow and pink horizontal bars) and experimental sessions (see the vertical colored bars in the right nodal distribution) along the conditioning process. Furthermore, note that in the right-hand dendrogram D2 for averaged blocks and in the right nodal distribution for sessions, the total number of significant clusters was of 10 groups -i.e., an insufficient number of clusters to match with 15 experimental conditioning sessions. Moreover, the threshold linkage distance was 117.94 units (see the vertical red dashed line) -i.e., a linkage distance that does not allow a valid rejection of the non-significant data corresponding to averaged blocks.

This strategy of the simulated causality conditions by a controlled random modification of the directionality and causality inferences (the parameters 36, 37, 39, and 40, which involved IP neuron interdependencies, Fig. 2a) in the temporal domains of the inter-trials and inter-sessions interactions strongly suggests that the proper timing of CRs is plausibly a consequence of the pertinent cerebellar-interpositus/red nucleus-motoneuron network causality -i.e., the simulated causal conditions affect the typical temporal distribution of training blocks and experimental sessions along the conditioning process, and therefore the temporal evolution of the level of expression of eyelid CRs. An additional advantage of this approach is that for the actual causality conditions, once collected data were properly arranged according to the hierarchical cluster tree (and that non-significant data were rejected), it was possible to determine the multiple and coherent evolution of the parameters (1-40) and the relationship between the causal inferences and phase-inversion properties of OO MNs and IP neurons with regard to acquired CRs. This phase-synchronization analysis demonstrates that causal inferences are dependent on the phase information status and that the timing of learned eyelid responses depends on the causal relationships present in the cerebellar-interpositus/red nucleus-motoneuron network.

3. Discussion

3.1. A more precise picture of the functional states involved in the actual acquisition of eyelid CRs

In a recent work from our group (Sánchez-Campusano et al., 2011a) we presented a quantitative statistical analysis of several separate but similar experiments in order to test the pooled data for statistical significance revealing how IP neurons can change their activity during delayed eyeblink conditioning. That previous meta-analysis enabled a comparison for learning and performance in different species (cats and wild-type and Lurcher mice). The present experimental design in alert behaving cats (for a single animal species) enables the incorporation of further parameters (timing information, time delays, time–intensity dispersion patterns, directionality in coupling, and causality indices) with the sole condition that the same experimental conditioning situation is reproduced (i.e., the same delay conditioning paradigm).

Although we have checked here the firing characteristics of only OO MNs and IP neurons, the intrinsic coherence demonstrated among timing information, kinetic and kinematic parameters, time delays and correlation code properties, time–intensity dispersion patterns, directional outcomes, and causality inferences conforming the forty-dimension vectors of learning states (Fig. 2a) strongly suggests the presence of a functional neuronal state involving many different cerebral centers evoked by the learning process (Delgado-García & Gruart, 2002; Sánchez-Campusano et al., 2011a,b).

In previous reports (Gruart et al., 1995; 2000; Sánchez-Campusano et al., 2007, 2009), we demonstrated by different means that neuronal activity in the IP neurons does not lead the performance of learned motor responses, but follows neural motor commands originated in different neuronal sources. Although it is highly speculative at the moment, we can suggest that a driving common source in motor cortex and/or in related cortical areas could act as both a trigger and a distributor of significant functional information in relation with the timing and performance of conditioned eyelid responses. As a whole, IP neurons could be considered to behave as a neuronal phase-modulating device supporting OO MNs firing during learned eyelid movements.
In this paper, the results of the causal analyses for the time-dependent relative variation functions of the IP neurons and OO MNs firing rates enabled investigation of the relationship between the relevance of spike timing and the novel spatiotemporal (De Zeeuw et al., 2011) patterning (as a neuronal state vector at the milliseconds timescale) characterizing the firing properties and their dynamic patterns (time-dispersion and temporal evolution), as well as the strength of the interdependencies between neuronal activities and the performance (kinematics) of eyelid conditioned responses. This idea was extended to inter-trials, inter-blocks (Fig. 2a), and inter-sessions (Fig. 2b) interactions of the datasets using the corresponding averaged firing rates of IP neurons and OO MNs and their causality interdependencies (all as a more exhaustive averaged spatiotemporal pattern) to study the timing of averaged eyelid CRs, the sequential temporal distribution of averaged datasets corresponding to averaged blocks and experimental sessions along the conditioning process.

Finally, the same experimental protocols and analytical procedures (including as an essential method the circular distribution of the experimental data) could also be applied to different durations of CS-US interval as an alternative approach to provide interval-based representations in order to understand better the interval timing mechanisms. In the first instance, the simulated time conditions where the data distribution is fitted to the circle may be extended to the standard interval timing strategy with the aim of exploring the quantifiable changes in the time–intensity dispersion patterns of data distributions depending on the duration of the CS-US interval.

In the second instance, these experimental and analytical tools could also be applied to many pharmacological manipulations that modify the spatiotemporal firing pattern (spike rate, spike timing, and correlation codes) within the cerebellar-interpositus/red nucleus-motoneuron network. These modifications in the spatiotemporal patterns lead to a dynamic change in the functional neuronal state (timing and their corresponding kinetic neural commands and dispersion patterns) evoked by the learning process, and consequently to some change in the timing and performance of the learned motor responses – i.e., in the motor behavior.

4. Conclusions

Collected data strongly suggest that the timing of eyelid CRs depends on causality in the cerebellar-interpositus/red nucleus-motoneuron network. Thus, we could propose a neural mechanism in which the firings of the cerebellar posterior interpositus neurons facilitate a quick repolarization process (by mean of phase modulation of the firing rates) of OO MNs, reinforcing their tonic firing during the performance of conditioned eyelid responses. Therefore, the cerebellar posterior IP neurons participate in the accurate timing and proper performance of the ongoing conditioned responses but not in their generation and/or initiation.

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References


