

Spontaneous eyeblinks are sensitive to sequential learning

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Highlights

- Dopamine regulates both sequential learning and spontaneous eyeblink rate (EBR)
- Participants performed a serial reaction time task (SRT) and EBR was recorded
- EBR decreases during SRT and increases with sequential irregularities
- Inter-individual differences in EBR and SRT performance are partly correlated
- EBR indirectly reflect dopaminergic activity coupled to sequential learning

Abstract

Although sequential learning and spontaneous eyeblink rate (EBR) have been both shown tightly related to cerebral dopaminergic activity, they have never been investigated at the same time. In the present study, EBR taken as an indirect marker of dopaminergic activity was investigated in two resting state conditions, both before and after visuomotor sequence learning in a serial reaction time task (SRT), and during task practice. Participants' ability to produce and manipulate their knowledge about the sequential material was probed in a generation task. We hypothesized that the time course of spontaneous EBR might follow the progressive decrease of RTs during the SRT session. Additionally, we probed the nature of the transfer blocks as well as their respective order, assuming that (1) fully random trials might generate a larger psychophysiological response than an unlearned but structured material, and (2) a delayed (last) block of transfer might give rise to larger effects given that the sequential material was better consolidated after further practice. Finally, we tentatively presumed that, in addition to their online version, spontaneous EBR recorded during the pre- and post-learning resting sessions might be predictive of (a) the SRT learning curve, (b) the magnitude of the transfer effects, and (c) performance in the generation task. Results evidenced successful sequence learning, with decreased accuracy and increased reaction times (RTs) in transfer blocks featuring a different material (random trials or structured, novel sequence). In line with our hypothesis that EBR reflects dopaminergic activity associated with sequential learning, we observed increased EBR in random trials as well as when the second transfer block occurred at the end of the learning session. There was a positive relationship between the learning curve (RTs) and the slope of EBR during the SRT session. Although inter-individual differences in resting and real-time EBR predicted the magnitude of accuracy and RTs transfer effects, respectively, they were not related to participants' performance during the generation task. Notwithstanding, our results suggest that the degree of explicit sequential knowledge modulates the association between the magnitude of the transfer effect in EBR and SRT performance. Overall, the present study provides evidence that EBR may represent a valid indirect psychophysiological correlate of dopaminergic activity coupled to sequential learning.

Keywords: spontaneous eyeblinks | sequential learning | serial reaction time | generation task
| dopamine

1. Introduction

Sequencing actions and perceptions is one of the most fundamental skills in everyday cognitive processing (Clegg, Digirolamo, & Keele, 1998; Conway & Christiansen, 2001; Dehaene, Meyniel, Wacongne, Wang, & Pallier, 2015; Janata & Grafton, 2003). It is now well documented that dopaminergic activity is a robust mediator of sequential processing (Berns & Sejnowski, 1998; Jin & Costa, 2015; Schultz, 2016). An extensive survey of the literature has pointed that spontaneous eyeblinks might be an indirect and a relevant marker of dopaminergic activity associated to a panel of cognitive functions such as attention, flexibility or inhibition (Jongkees & Colzato, 2010). However, to the best of our knowledge, no study investigated the potential relationship between sequential learning and spontaneous eyeblinks. It is quite surprising given their respective linkage with dopaminergic activity.

Since Nissen and Bullemer (1987)'s seminal study, sequential learning has been largely investigated using a relatively simple paradigm: the serial reaction time task (SRT; for a review see Schwarb & Schumacher, 2012; Schwarting, 2009). In the original study, participants faced a computer screen displaying four horizontal fixed locations. All along the experimental protocol, participants had to press as fast and accurately as possible on a spatially compatible response key when a visual stimulus appeared above one of the four locations. Unknown to them, the sequential display of the stimuli followed a hidden and recurrent sequence of ten positions (4231324321, each number representing a location on the screen). Results showed that, compared to participants exposed to random trials, participants exposed to the structured material became gradually more accurate and responded faster. Performance improvement was interpreted as resulting from the sequential learning of the regularities, allowing participants to anticipate the next stimulus location. Nonetheless, participants were found unable to verbally reproduce the sequence at the end of the session, suggesting that learning was implicit (Curran & Keele, 1993; Willingham, Nissen, &

Bullemer, 1989). Several methodological refinements and variations were brought to the SRT paradigm. In further studies, a block of random trials or a block made from another, unlearned sequence was presented to the participants at the end of the learning session, as a way of measuring sequence learning at the within-subject level (e.g., Cohen, Ivry, & Keele, 1990; Reed & Johnson, 1994). Participants' reaction times (RTs) increased when confronted to the novel material (i.e., a transfer effect), suggesting sensitivity to the violation in the structure of a previously learned material. Another variation is the probabilistic SRT (e.g., Cleeremans & McClelland, 1991; Jiménez, Méndez, & Cleeremans, 1996) in which the sequence of the stimuli is governed by an artificial grammar made from a complex set of rules defining the legal transitions between successive stimuli ("grammatical" stimuli). While most of the material is generated based on the finite-state grammar, some transitions (typically, 10%) are random ("non-grammatical") and hence violate the rules. In such a situation, participants' RTs become gradually faster for grammatical as compared to non-grammatical stimuli all along the learning session, suggesting an ongoing enhancement of motor response preparation towards the most predictable stimuli. As a variant, the alternating SRT task (ASRT; Howard & Howard, 1997) is a combination of deterministic and probabilistic SRT in which the elements of a fixed sequence alternate with random trials (e.g., 1r4r3r2r1r4r3r2r). During the learning session, participants' accuracy and/or RTs associated to random trials respectively decrease and slow down, as compared to the trials belonging to the sequence. Again, this pattern clearly suggests behavioral sensitivity towards sequential regularities.

The validity of verbal reports assessing participants' knowledge about the sequential structure of the material learned during practice was also questioned (Shanks & St. John, 1994). In particular, it may be the case that finding that people have little verbalizable knowledge of the sequential regularities may simply reflect a bias towards not reporting

knowledge held with low confidence, rather than the presence of genuinely unconscious knowledge. This observation led to the development of more sophisticated methods to evaluate participants' awareness (for a review see e.g., Destrebecqz & Peigneux, 2005). For instance, recognition tasks in which participants must decide whether sequential fragments (e.g., chunks of three successive elements) belong or not to the learned sequence have been used as a better estimate of conscious sequential knowledge (e.g., Perruchet & Amorim, 1992). Alternatively, some authors have pointed out the advantage of using so-called "generation tasks" (e.g., Jiménez et al., 1996; Shanks & Johnstone, 1999), in which participants must actively generate the learned sequence or what they think it was. Therefore, comparing the number of generated familiar chunks against chance level can provide an index of conscious knowledge. However, performance on generation tasks can rest not only on explicit knowledge about the sequence, but also on a mere familiarity with the succession of locations. In this framework, applications of the Process Dissociation Procedure (PDP; see Jacoby, 1991) have been developed to disentangle the contributions of explicit and implicit processes in generation performance (e.g., Destrebecqz & Cleeremans, 2001; Schmitz, Pasquali, Cleeremans, & Peigneux, 2013). Indeed, during the classical generation task, in which participants must reproduce the learned sequence (an "inclusion" condition in the PDP framework), both explicit and implicit knowledge of the sequence can contribute to performance and generation of the learned chunks. However, when participants are requested to generate a different sequence or the reverse sequence they had learned (i.e., an "exclusion" condition), then only explicit knowledge allows them to control and intentionally avoid producing previously learned elements. Therefore, in the Exclusion condition, if learned chunk elements are unintentionally generated above chance level, this can be interpreted as the influence of implicit processes that cannot be controlled by

conscious knowledge; thus evidencing implicit sequence learning (Destrebecqz & Cleeremans, 2001; Destrebecqz & Peigneux, 2005).

In the current study, we aimed at evaluating the relationships between sequential learning and spontaneous eye blink rate (EBR) given their respective link to dopaminergic activity. Indeed, numerous human and animal studies showed that EBR is a valid and reliable marker of striatal dopaminergic activity (for an extensive review see Jongkees & Colzato, 2016). For instance, Parkinson's disease, a neurological disorder characterized by a loss of striatal dopamine, is associated with decreased EBR (e.g., Agostino, Berardelli, Cruccu, Stocchi, & Manfredi, 1987; Agostino et al., 2008; Karson, 1983; Karson, Burns, LeWitt, Foster, & Newman, 1984; Karson, LeWitt, Calne, & Wyatt, 1982) that can be reversed after L-DOPA treatment restoring dopamine levels (Karson, 1983; Karson, Burns, et al., 1984). On the other hand, schizophrenic patients blink more than control participants (e.g., Helms & Godwin, 1985; Karson, Berman, Kleinman, & Karoum, 1984; Mackert, Woyth, Flechtner, & Frick, 1988), which is generally interpreted as the result of a hyperdopaminergic state (see Jongkees & Colzato, 2016). Corroborating this explanation, dopaminergic antagonists reduce EBR in schizophrenic patients (e.g., Adamson, 1995; Mackert et al., 1988), which parallels improved symptomatology (Bartko, Herczeg, & Zador, 1990; Karson, Bigelow, Kleinman, Weinberger, & Wyatt, 1982). Noticeably, beyond methodological differences between studies, both Parkinson and schizophrenic patients often exhibit impaired sequence learning in different versions of the SRT (for reviews see Clark, Lum, & Ullman, 2014; Remillard, 2014; Ruitenberg, Duthoo, Santens, Notebaert, & Abrahamse, 2015; Siegert, Taylor, Weatherall, & Abernethy, 2006; Siegert, Weatherall, & Bell, 2008). Furthermore, PET scan studies using ^{11}C -raclopride, a D2 dopamine receptor radioligand, evidenced increased striatal dopaminergic activity in healthy participants during a learning session both in deterministic (Badgaiyan, Fischman, & Alpert, 2007, 2008; Lappin et al., 2009) and probabilistic (Garraux,

Peigneux, Carson, & Hallett, 2007) SRT. In addition, implicit and explicit generation scores following a deterministic SRT were associated to inter-individual differences in spontaneous D2 dopaminergic activity during a resting state ^{11}C -raclopride PET scan (Karabanov et al., 2010). In line with these results, previous H_2^{15}O PET studies pointed out a predominant role of striatal activity in the acquisition of probabilistic regularities (Peigneux et al., 2000), an activity modulated during a sequence generation task after deterministic sequence learning (Destrebecqz et al., 2003, 2005). Further, genetic markers of spontaneous striatal dopaminergic activity interact with aging and impact the learning curve in a deterministic SRT (Schuck et al., 2013). Animal experiments using pharmacological and lesion studies confirmed the involvement of striatal dopaminergic activity in a rodent adaptation of the SRT paradigm (for a review see Schwarting, 2009). Overall, these data suggest a crucial involvement of striatal dopaminergic activity in both sequential learning and spontaneous EBR. Therefore, spontaneous EBR might be modulated by, or be predictive of performance in the SRT and/or the generation task, thus indirectly reflecting dopaminergic activity coupled to sequential learning.

In the present study, spontaneous EBR was recorded as an indirect marker of intrinsic dopaminergic cerebral activity (Jongkees & Colzato, 2016) during two resting state sessions set immediately before and after a sequence learning session, while participants were practicing a deterministic SRT (Destrebecqz & Cleeremans, 2001). We tested (1) whether the evolution of spontaneous EBR would match a typical deterministic SRT learning session, and/or, at a more exploratory level, (2) how EBR would be affected by, and related to transfer effects. Firstly, we hypothesize that the time course of spontaneous EBR might follow the progressive decrease of RTs during the SRT session (Badgaiyan et al., 2007, 2008; Lappin et al., 2009; Garraux et al., 2007). Therefore, an intercorrelation between their respective learning curve might be expected. Additionally, we hypothesized that the nature of the

transfer blocks, as well as their respective order, might induce different psychophysiological responses. Indeed, random trials might generate a larger psychophysiological response than an unlearned but structured material (i.e., a new sequence), as suggested by neuroimaging studies showing higher striatal activity for random compared to sequential material (e.g., Poldrack et al., 2005; Schendan, Searl, Melrose, & Stern, 2003). Furthermore, it can be expected that the last block of transfer will give rise to larger effects given the better consolidation of the sequential material after further additional regular blocks of practice (e.g., Meier & Cock, 2014; Tzvi, Stoldt, Witt, & Kramer, 2015). Finally, and at a more exploratory level, we assumed that, in addition to their online version, spontaneous EBR recorded during the pre- and post-learning resting sessions might be predictive of (a) the SRT learning curve, (b) the magnitude of the transfer effects, and (c) the number of chunks produced in the Inclusion and Exclusion conditions of a generation task (Karabanov et al., 2010).

2. Material and methods

2.1. Participants

Thirty-three young healthy volunteers (22.2 ± 2.9 years old, 17 males) gave their written informed consent to participate in this study approved by the Faculty Ethics committee. Initially the study involved 36 participants but three of them had to be discarded because of electrooculogram (EOG) signal loss and/or the presence of too many artifacts within the recording. All participants were non-musicians and right-handed as assessed by the French version of the FLANDERS questionnaire ($9.5 \pm .9$, range from 7 to 10; Nicholls, Thomas, Loetscher, & Grimshaw, 2013). Sleep quality for the month prior to the experiment was assessed using the Pittsburgh Sleep Quality Index (PSQI; Buysse, Reynolds, Monk, Berman, & Kupfer, 1989): use of sleeping pills and bad sleep quality were exclusion criteria (PSQI global score > 8). Participants were screened to have neutral to moderate chronotypes (range

34-63 on the Morningness-Eveningness Questionnaire; Horne & Ostberg, 1976). At the time of testing, all participants had normal vision or wore corrective glasses when needed. Lenses were not allowed to avoid any interference with spontaneous eyeblinks recording.

2.2. Tasks and materials

Behavioral testing was carried out on a PC system with a 18.5” width screen, using a Cogent 2000 routine (<http://www.vislab.ucl.ac.uk>) implemented on Matlab R2014a.

2.2.1. Serial Reaction Time task

The display consisted of six permanent white lines positioned horizontally on a black background (see Figure 1). Each line was matched with a key (S, D, F, J, K and L) on a PC azerty keyboard. The spatial configuration of the keys and fingers corresponded to the screen positions. The target stimulus was a white circle that appeared above one of six permanent white lines. During the SRT task, participants had to press as fast and as accurately as possible on the key corresponding to the target stimulus which remained on screen until a response was given. Response-stimulus interval was fixed at 250 ms. The two sequences consisted of so-called “second order conditional” transitions (SOC; Reed & Johnson, 1994). In other words, with SOC sequences, two elements of temporal context are always necessary to predict the location of the next stimulus. It should be noted that the two sequences used here preserve a SOC property when they are reversed (i.e., when read from right to left). Further, the original sequence did not share any common transitions with its reverse. The main interest of using reverse SOCs is that Exclusion instructions are simplified to a considerable extent, since participants can merely be asked to produce the training sequence in reverse (Pasquali, Cleeremans, & Gaillard, 2018; Schmitz et al., 2013; see the next section). Unknown to participants, 18 out of the 20 SRT training blocks contained 8 repetitions of the same 12-elements sequence governing the apparition of the target stimuli.

These 18 blocks (B1-10, B12-15 and B17-20) were ruled by one of the two possible sequences (SOCa: SOC1 = 531624152364 vs. SOC2 = 461325142635). In order to assess transfer effects, the 11th and 16th blocks were made either from the second, unlearned sequence (SOCb: SOC2 = 461325142635 vs. SOC1 = 531624152364, respectively) or from 96 random trials, different for each participant (with the only exception that no immediate repetition was allowed). For half of the participants the block made with the unlearned sequence appeared first, before the random block (SOCb/Rand) whereas the other half was presented first the random block (Rand/SOCb).

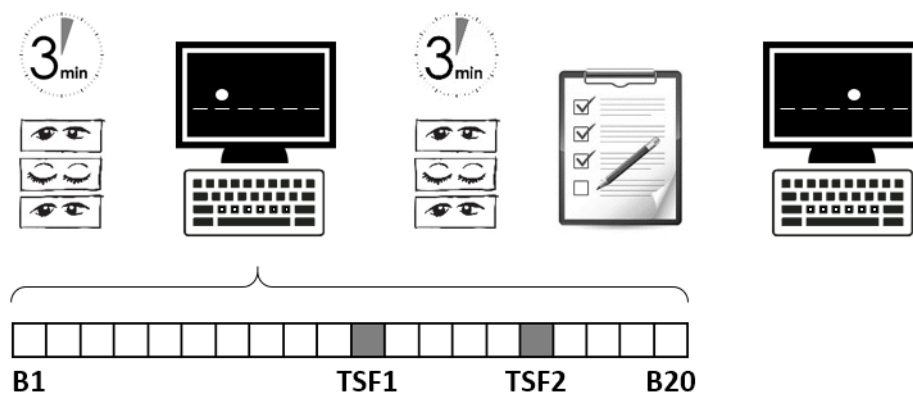


Figure 1. Timeline of the experimental protocol. **Top.** 3 minutes of resting state (passive eyeblinks recording) followed by a learning session of SRT (blocks B1 to B20) and a second resting state of 3 minutes. Immediately after, participants complete a sleep questionnaire. The generation task (inclusion and exclusion conditions) ends the protocol. **Bottom.** The learning session was composed of 20 blocks each composed of 8 repetitions of a sequence of 12 items (SOCa), except for the blocks B11 and B16 (grey squares = transfer blocks, TSF1 and TSF2, featuring either another sequence of 12 items, SOCb, or random trials, counterbalanced across two groups).

2.2.2. Generation task

Before performing the generation task, participants were informed that the dot stimulus did not move randomly but instead followed a recurrent pattern. They were then presented with the same display and asked to actively generate a series of 96 key presses that matched as best as possible the previously learned sequence (i.e., the Inclusion condition). They were

told to rely on their intuition whenever they felt unable to recollect the location of the next stimulus. After the Inclusion condition, participants were asked to generate the reverse pattern of the previously learned sequence for another 96 trials (i.e., the Exclusion condition). In both sessions, the first circle was randomly displayed at one of the six locations, and participants had to press one of the six corresponding keys to generate the next stimuli. Each stimulus appeared on screen immediately after each key press.

2.2.3. Eyeblinks recordings

A Morpheus recorder system (Micromed, Treviso, Italy) was used to record eyeblinks and horizontal and vertical eye movements. Eye movements were recorded with Ag–AgCl electrodes placed above and below the left eye (vertical eye movements and eyeblinks detection), and laterally to the external canthi (horizontal eye movements detection). The EOG was recorded all along the SRT protocol (from block B1 to B20) and for two 3-minutes resting conditions recorded before the first and after the last SRT block (see Figure 1). The resting state conditions were explained to each participant as a calibration needed for EOG recording and future processing, whereas the continuous EOG recording was presented as a simple measure to check their eye movements throughout the SRT task. During the resting state condition, participants were comfortably sitting 60 cm in front of the computer screen displaying a white cross on its center. They were asked to look at the cross in a relaxed and comfortable position and to avoid large eye and body movements. Given that spontaneous EBR is supposed to be stable during daytime but increases in the evening (circa 20:30, see Barbato et al., 2000), data were never collected after 18:00. Additionally, participants were asked to avoid any psychotropic consumption and to sleep sufficiently the day before.

2.3. Procedure

Each participant was tested individually in a quiet room. They were asked to stand still and keep a constant distance (60 cm) from the computer screen during all the experiment. They started first with a 3-min resting state condition followed by 20 blocks of SRT task. All along the SRT session, they were asked to respond as fast as possible to targets while keeping their accuracy score above 90%. At the end of each block, a feedback related to participants' speed and accuracy on the SRT task was automatically displayed. A second resting state condition of 3 minutes was proposed immediately at the end of the SRT task, which was followed by the completion of sleep questionnaires. After that, participants were instructed that the apparition of the stimuli was not random but followed a specific rule and the generation task was proposed. The Exclusion condition always followed the Inclusion condition. The entire experimental session lasted approximately 1 hour depending on participants' speed.

3. Results

The percentage of correct motor responses, the median RT associated to correct responses and the EBR were computed for each participant and each block of the SRT task and the two resting states (see Figure 2, Table 1 and Table A.1). Eyeblinks were individually and manually scored after visual inspection using BrainRT™ analysis software (OSG, Rumst, Belgium). EBR was computed as the number of eyeblinks divided either by the duration required to complete the corresponding block of SRT, or by the duration of the resting state session. The two transfer effects were computed as a delta score between each block of transfer and the preceding regular block (i.e., $TSF1 = B11 - B10$ and $TSF2 = B16 - B15$). The percentage of triplets belonging to the learned and reverse sequences was computed for the Inclusion and Exclusion conditions. Statistical analyses were performed with Statistica 10 (StatSoft, Inc.), except for the Bayesian factors (BF) analyses, which were computed with JASP (version 0.8.5.1, <http://jasp-stats.org>). It should be noted that while the vast majority of

studies using the deterministic SRT did not take into account the counterbalancement of the sequence in their statistical analyses, we decided to include this factor (i.e., SOC1 vs. SOC2) in the following sections given the potential impact of sequential structure on the extent to which learning may become explicit (Cohen et al., 1990; DeCoster & O'Mally, 2011; Reed & Johnson, 1994; Seger, 1997; Vaquero, Jimenez, & Lupianez, 2006; Wilkinson & Shanks, 2004).

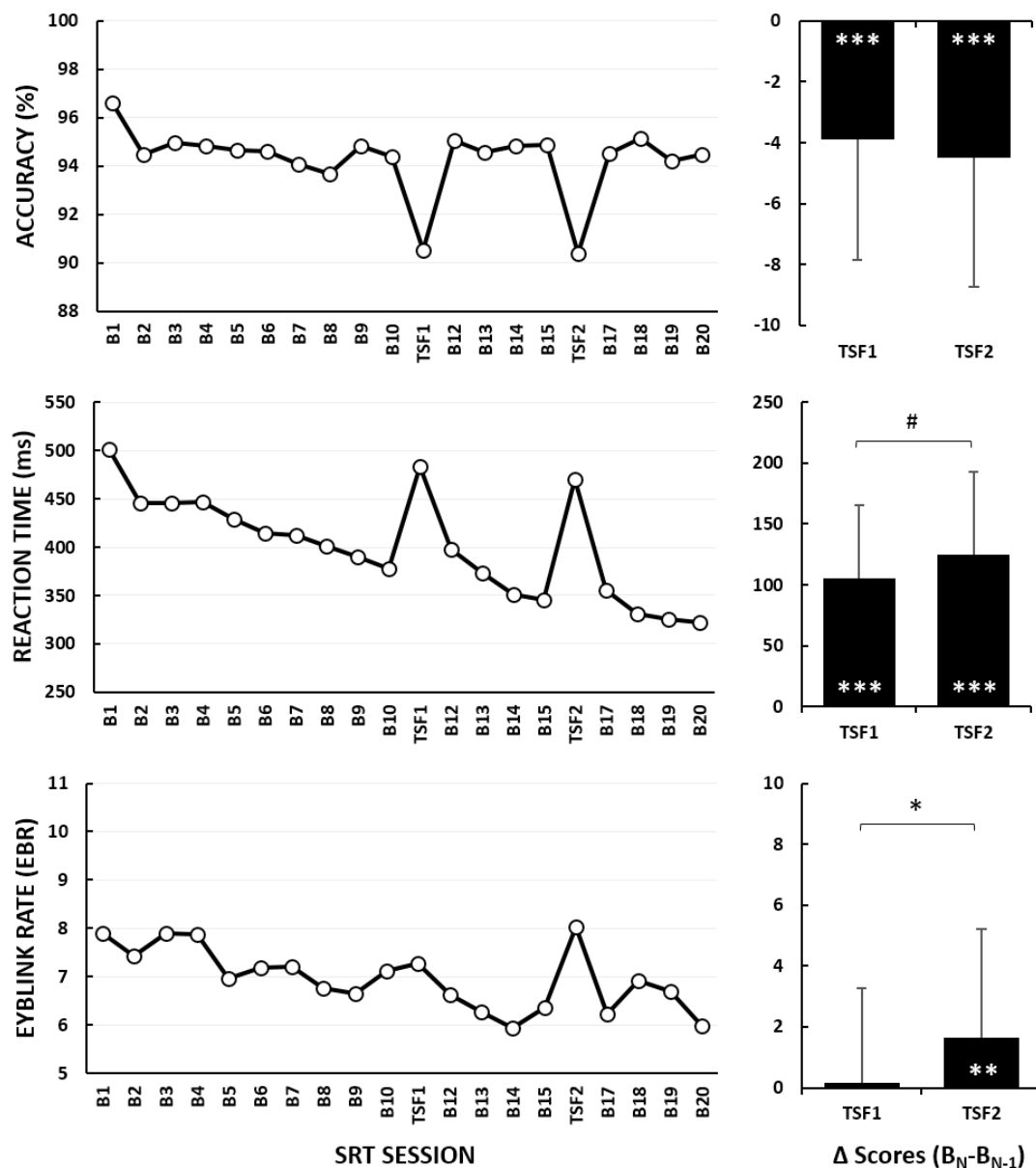


Figure 2. Accuracy (top, expressed in % correct), median RTs (middle) and EBR (bottom) for each block of the experimental session (left) and transfer effect (right). One-tailed t-tests against the value 0: (**) $p < .01$ and (***) $p < .001$. Main effect of Time of Transfer (TSF1 vs. TSF2): (*) $p < .05$ and (#) $p = .075$. Error bars represent standard deviations.

Table 1 – One-tailed Sample T-Test against 0 for each transfer effect

Transfer Effect ($B_N - B_{N-1}$)		Mean (SD)	$t_{(32)}$	p	Cohen's d	BF_{10}
Accuracy (%)	TSF1	-3.88 (3.95)	-5.65	< .001	.98	$1.27 \cdot 10^4$
	TSF2	-4.48 (4.24)	-6.07	< .001	1.06	$3.89 \cdot 10^4$
	RAND	-5.24 (4.21)	-7.15	< .001	1.24	$6.89 \cdot 10^5$
	SOCb	-3.13 (3.71)	-4.85	< .001	.84	$1.47 \cdot 10^3$
RTs (ms)	TSF1	105 (60)	10.03	< .001	1.75	$8.85 \cdot 10^8$
	TSF2	124 (68)	10.52	< .001	1.83	$2.72 \cdot 10^9$
	RAND	133 (66)	11.60	< .001	2.02	$2.98 \cdot 10^{10}$
	SOCb	96 (58)	9.54	< .001	1.66	$2.80 \cdot 10^8$
EBR (EB/min)	TSF1	.2 (3.3)	.30	0.38	0.05	.24
	TSF2	1.7 (3.7)	2.59	0.007	0.45	6.32
	RAND	1.6 (3.9)	2.32	0.014	0.40	3.73
	SOCb	.3 (3.0)	.46	0.32	0.08	.28

Note: The alternative hypothesis specifies the mean is either less (Accuracy) or more (RTs and EBR) than 0

3.1. SRT Task

A mixed ANOVA with Time of Transfer (TSF1 vs. TFS2) as within-subjects factor and Learned Sequence (SOC1 vs. SOC2) and Transfer Order (SOCb/Rand vs. Rand/SOCb) as between-subjects factors was computed on accuracy and RTs delta scores (TSF1 = B11 – B10 and TSF2 = B16 – B15). One-tailed t-tests were also computed against the value 0 (see Figure 2, Table 1 and Table A.1). Considering RTs, the mixed ANOVA disclosed a marginally significant main effect of Time of Transfer ($F_{(1,29)} = 3.42$, $p = .075$). The amplitude of the second transfer block tended to be higher than the first one (TSF2: 125 ± 68 ms vs. TSF1: 105 ± 60 ms). Regarding accuracy, the mixed ANOVA revealed a significant Time of Transfer by Transfer Order interaction ($F_{(1,29)} = 7.64$, $p < .01$), but Bonferroni post-hoc tests were non significant (all $ps > .11$). One-tailed t-tests against the value 0 revealed a highly significant transfer effect both on accuracy and RTs for all blocks of transfer across all participants, but also according to Time of transfer (TSF1 vs. TFS2), Transfer order

(SOCb/Rand vs. Rand/SOCb) and Sequence (SOC1 vs. SOC2) conditions ($.05 > ps > .0001$; see Figure 2, Table 1 and Table A.1).

3.2. Eyeblink Rate

A mixed ANOVA with Time of Transfer (TSF1 vs. TFS2) as within-subjects factor and Learned Sequence (SOC1 vs. SOC2) and Transfer Order (SOCb/Rand vs. Rand/SOCb) as between-subjects factors was computed on EBR delta scores (TSF1 = B11 – B10 and TSF2 = B16 – B15). One-tailed t-tests were also computed against the value 0 (see Figure 2, Table 1 and Table A.1). The mixed ANOVA evidenced a significant main effect of Time of Transfer ($F_{(1,29)} = 4.90, p = .035$); participants had a higher EBR during the second than the first block of transfer (TSF2: 1.65 ± 3.67 vs. TSF1: $.17 \pm 3.30$; see Figure 2). The Time of Transfer by Transfer Order interaction tended to be significant ($F_{(1,29)} = 4.06, p = .053$). Bonferroni post-hocs indicated a difference between the two blocks of transfer when the random block appeared in the second position (TSF1: $-.70 \pm 3.49$ vs. TSF2: 2.20 ± 4.74 ; $p = .037$). No difference between the two blocks of transfer was evidenced for the Rand/SOCb condition (TSF1: $.99 \pm 2.99$ vs. TSF2: 1.13 ± 2.30 ; $p = 1$). The ANOVA showed a significant Sequence by Transfer Order interaction ($F_{(1,29)} = 6.86, p = .013$) but no Bonferroni posthocs was significant (all $ps > .05$). No other main effect or interaction reached statistical significance (all $ps > .19$). The one-tailed t-tests against the value 0 revealed a significant transfer effect on EBR across all participants for the second ($p = .007, BF_{10} = 6.32$) but not for the first block of transfer ($p > .38, BF_{10} = .24$; see Figure 2, Table 1 and Table A.1). T-tests also evidenced a significant transfer effect on EBR across all participants when the block of transfer was random ($p = .014, BF_{10} = 3.73$) but not when it was made from another sequence, SOCb ($p > .32, BF_{10} = .28$; see Table 1). For information, one-tailed t-tests against the value 0 are also reported in Table A.1 according to the learned sequence (SOC1 vs. SOC2); they replicate the pattern of results only in participants who had to learn the SOC2.

A mixed ANOVA with Time (REST1 vs. B1 vs. B20 vs. REST2) as within-subjects factor and Learned Sequence (SOC1 vs. SOC2) and Transfer Order (SOCb/Rand vs. Rand/SOCb) as between-subjects factors was computed on EBR to evaluate the time course of EBR during both resting state sessions and the beginning and the end of the SRT session. The analysis revealed a highly significant effect of Time ($F_{(3,87)} = 6.03, p < .001$; see Figure 3). Bonferroni post-hocs showed that EBR during the first resting state session was higher (REST1: 11.35 ± 6.01) than EBR recorded during blocks B1 ($7.99 \pm 6.97; p = .045$) and B20 ($6.30 \pm 7.06 \%; p < .001$), but did not differ from the second resting state session (REST2: $9.34 \pm 5.61; p > .62$). EBR in the last resting state session tended to be higher than B20 ($p = .091$) but did not differ significantly from B1 ($p = 1$). No other main effect or interaction reached statistical significance (all $ps > .20$).

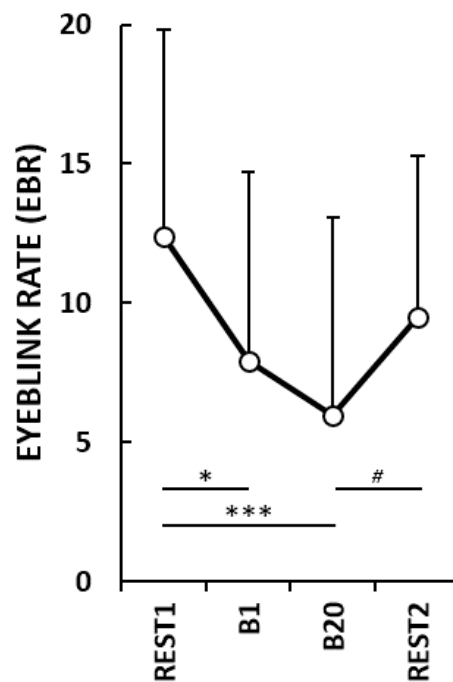


Figure 3. Eyeblink Rate (EBR) recorded during the resting state before (REST1) and after (REST2) the SRT session, and during the first (B1) and last (B20) blocks of SRT. Bonferroni post-hocs: (*) $p < .05$, (***) $p < .001$ and (#) $p = .091$. Error bars represent standard deviations.

3.3. Generation Task

Generation performance was computed as the number of generated 3-elements chunks all along the 96 trials belonging to the training sequence or its reverse. Chance level was set at 10% of generated triplets: 12 possible triplets in the SOC and 120 (6*5*4) possible triplets within a sequence with 6 possible locations (i.e., random level = 12/120 = 10%; see Figure 4, for more detailed results see Table 2).

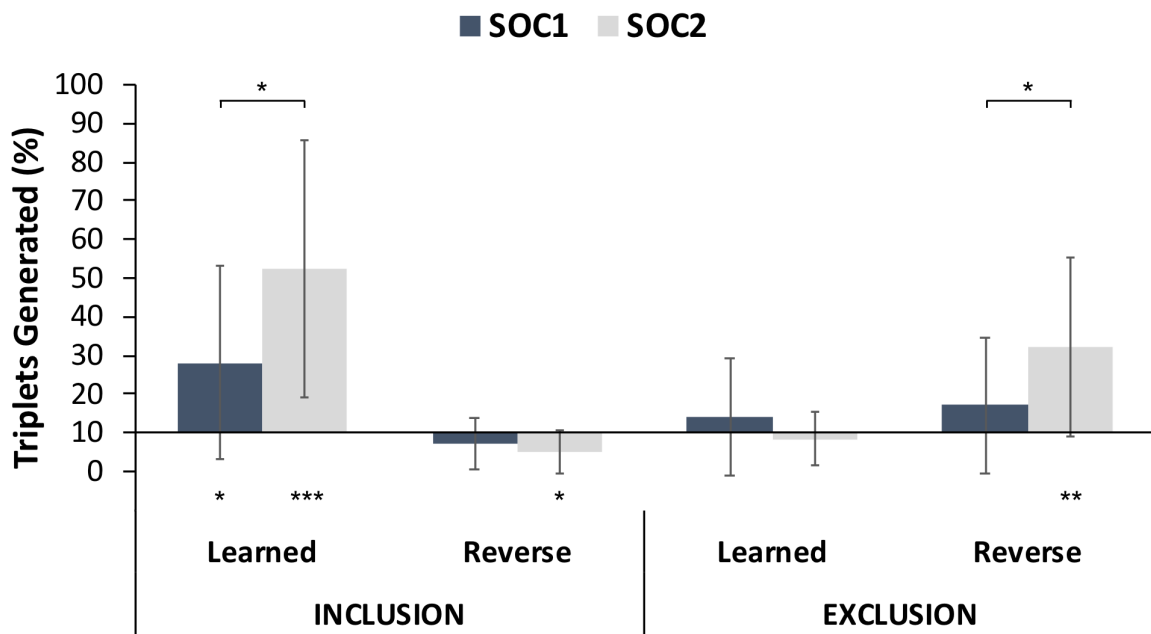


Figure 4. Generation scores (proportion of generated triplets belonging to the learned or the reverse sequences) for SOC1 and SOC2 groups according to the Inclusion and Exclusion instructions. Chance level was set at 10%. T-tests against the value 0: (*) $p < .05$, (**) $p < .01$ and (***) $p < .001$. Planned comparisons (SOC1 vs. SOC2): (*) $p < .05$. Error bars represent standard deviations.

Table 2 – Proportion (%) of generated triplets according to each SOC group and generation condition							
			Mean (SD)	t	<i>p</i>	Cohen's <i>d</i>	BF ₁₀
SOC1 (n = 16)	INCLUSION	Learned	28.12 (25.12)	2.89	.011	.72	4.95
		Reverse	7.34 (6.68)	-1.61	.129	.40	.74
	EXCLUSION	Learned	14.03 (15.02)	1.07	.30	.27	.42
		Reverse	17.29 (17.56)	1.66	.118	.42	.79
SOC2 (n = 17)	INCLUSION	Learned	52.57 (33.27)	5.27	<.001	1.28	363
		Reverse	5.19 (5.49)	-3.61	.002	.87	18.19
	EXCLUSION	Learned	8.51 (6.71)	-.92	.37	.22	.36
		Reverse	32.23 (23.25)	3.94	.001	.96	33.09

Note: The alternative hypothesis specifies the mean is different than 10 (chance level)

A mixed ANOVA with Instruction (Inclusion vs. Exclusion) and Nature of Triplets (Learned vs. Reverse sequence) as within-subjects factors and Learned Sequence (SOC1 vs. SOC2) and Transfer Order (SOCb/Rand vs. Rand/SOCb) as between-subjects factors was computed on the proportion of the generated triplets. The analysis revealed significant main effects of Instruction ($F_{(1,29)} = 12.07, p < .01$), Nature of Triplet ($F_{(1,29)} = 19.45, p < .001$) and Sequence ($F_{(1,29)} = 4.82, p = .036$), a significant Instruction by Sequence ($F_{(1,29)} = 4.55, p = .041$) and Instruction by Nature of Triplet ($F_{(1,29)} = 27.66, p < .0001$) interactions, and, lastly, a significant triple interaction of Instruction by Sequence by Nature of Triplet ($F_{(1,29)} = 6.98, p = .013$). Planned comparisons showed that SOC1 and SOC2 groups differed for the proportion of the learned triplets in the Inclusion condition ($p = .019, d = .83, BF_{10} = 5.13$), and for the proportion of reverse triplets in the Exclusion condition ($p = .033, d = .72, BF_{10} = 3.16$; see Figure 4).

A series of two-sided t-tests against chance value (i.e., 10%) was performed on the proportion of the learned and reverse triplets in the Inclusion and Exclusion conditions for SOC1 and SOC2 groups. In the Inclusion condition, each group produced above chance level

a proportion of chunks belonging to the learned sequence (both $ps < .05$), whereas the number of reverse triplets was under chance level for the SOC2 group ($p < .01$; see Figure 4 and Table 2). In the Exclusion condition, only the SOC2 group was able to generate a percentage of reverse triplets above chance level ($p < .01$) while the number of learned triplets did not differ to chance level for the two groups (both $ps > .25$; see Figure 4 and Table 2).

Four distinct repeated measures ANOVAs with Triplet (Triplet 1 to Triplet 12) as within-subjects factors were computed for each learned SOC group (SOC1 vs. SOC2) to determine whether participants generated some triplets more than another according to the generation instructions (Inclusion vs. Exclusion). Analyses revealed a main effect of Triplets in the SOC2 group in the Inclusion ($F_{(11,187)} = 4.69, p < .0001$) and Exclusion ($F_{(11,187)} = 2.48, p < .01$) conditions. No significant effect was evidenced for the group who learned the SOC1 (both $ps > .25$). Bonferroni post-hocs revealed that the 2nd and the 3rd triplets of the SOC2 (461325142635) were more often generated in the Inclusion condition than other triplets (see Table B.1). Post-hocs failed to disclose any significant difference between triplets in the Exclusion condition.

Overall, statistical analyses indicate that participants in SOC1 and SOC2 groups generated a significant number of learned triplets in the Inclusion condition. In addition, participants in the SOC2 group were also able to use their knowledge about the learned sequence to explicitly generate its reverse, contrary to the SOC1 group, who remained at chance level.

3.4. Correlational analyses

Pearson correlations were performed to assess a potential association between EBR in both sessions of resting state and the transfer effect delta scores (TSF1 = B11 – B10 and TSF2 =

B16 – B15) for the accuracy, RTs and EBR recorded during the SRT task. Transfer effects were computed separately according to the order (TSF1 vs TSF2) and the nature of the transfer blocks (random vs. new sequence, SOCb). Correlations by group were also performed according to the sequence participants had to learn (SOC1 vs. SOC2), given the observed difference in conscious knowledge between the two groups. All the results are reported in detail in Table C.1. In the following, we will only report (see Figure 5) and discuss robust correlations justified by substantial Bayes factors (i.e., $BF_{10} > 3$; see Dienes, 2011).

Across the entire group, EBR in the first resting state session was negatively correlated with transfer accuracy observed in the first transfer block ($r_{(32)} = -.42, p < .05; BF_{10} = 3.93$), but also with transfer accuracy when the block of transfer was made from random trials ($r_{(32)} = -.43, p < .05; BF_{10} = 4.44$). In other words, participants who blinked the most during the first resting session were the less accurate during the first block of transfer, or when they were performing a random block. Interestingly, the EBR and RTs transfer effect presented a negative relationship during the random block of transfer ($r_{(32)} = -.43, p < .05; BF_{10} = 4.61$). Participants whose EBR decreased the most during the random block were those who had the highest RTs transfer effect. At last, analyses revealed a relatively good consistency between the two EBR resting sessions ($r_{(32)} = .53, p < .01; BF_{10} = 25.70$). Each of these results remained unchanged for the participants who had to learn the SOC2 (all $ps < .05$ and $BF_{10} > 3$), at variance with the SOC1 group in which no association was found with EBR (all $ps > .05$ and $BF_{10} < 3$; see Figure 5 and Table C.1).

Additional correlations were computed to test the relationship between the generation scores in the Inclusion and Exclusion conditions and EBR. No significant correlation was found in all participants or according to the learned sequence (all $ps > .05$ and $BF_{10} < 3$). Additionally, individual linear regressions were computed on RTs and EBR associated to the first ten blocks in order to modelize and correlate their respective slope (i.e., the time course of these two parameters). The remaining blocks were excluded to avoid any contamination of the two blocks of transfer. The analysis revealed a significant positive correlation between RTs and EBR slopes ($r_{(32)} = .40, p = .011; BF_{10} = 5.41$), suggesting a relative parallelism between RTs and EBR evolution during the first part of the learning session (see Figure 2). Finally, EBR in the first and the second resting state sessions were both correlated with RTs and EBR slopes extracted from the SRT session. A significant correlation was found between the first EBR resting session and the RTs slope ($r_{(32)} = .45, p = .009; BF_{10} = 5.54$), suggesting

that higher EBR was associated with a steeper learning slope. It should be noted that the EBR slope also negatively correlated with the first EBR resting session ($r_{(32)} = .35, p = .046$) but this result was anecdotal according to the bayesian analysis ($BF_{10} = 1.46$). The other correlations did not reach significance (all $ps > .05$ and $BF_{10} < 3$).

4. Discussion

The aim of our study was to investigate whether spontaneous EBR was sensitive to sequential learning and/or predictive of the gained sequential knowledge, given their respective dependency to cerebral dopaminergic activity. To do so, EBR was recorded through two resting sessions taking place before and after the main sequence learning task, as well as online during the entire learning session of a deterministic SRT. In addition, participants had to perform a generation task in which they had to reproduce the trained sequence (under inclusion instructions) and its reversal (under exclusion instructions). Our main result shows that the time course of EBR recorded during the SRT followed participants' RTs learning curve. Our data also reveal an EBR transfer effect after sufficient learning has taken place: EBR significantly increased during the second block of transfer, that is, when the stimulus was not following the sequential regularities anymore. The random block was also specifically associated to increased EBR as compared to a block consisting of another sequence (i.e., SOCb), and the inter-individual EBR variability recorded during the random block was related to the magnitude of the RT transfer effect. Interestingly, resting EBR recorded before the SRT session was predictive of accuracy during the first transfer block (independently from its nature, TSF1) and during the block composed of random trials (independently of its position within the learning session). The transfer effect observed on EBR appears to be modulated by the sequential knowledge acquired by the participants. Indeed, additional exploratory analyses revealed that the internal structure of the SOC2 might have primed an intentional learning mode during the SRT session. This could explain why

participants who learned this sequence succeeded on the Exclusion condition of the generation task, compared to the SOC1 group, but also why the EBR effects associated to SRT performance were mainly — if not exclusively — observed in the SOC2 group. Lastly, no relationship was evidenced between EBR and the generation scores. Each of these results will be discussed point by point in the following paragraphs.

The correlation between the RTs and EBR slopes fits well with a ^{11}C -raclopride PET study showing a close interrelationship between pallidal, frontal and premotor dopaminergic activity and the slope modelling the progressive differentiation among grammatical and non-grammatical stimuli during a learning session in a probabilistic SRT (Garraux et al., 2007). Accordingly, the time course of EBR during SRT could reflect the progressive consolidation of the sequential structure. In our study, the transfer effect on EBR paralleling the RTs on the second block of transfer would also be in agreement with this hypothesis. This is also in line with two other ^{11}C -raclopride PET studies showing an increased dopaminergic activity in striatal areas when participants started to perform a deterministic SRT (Badgaiyan et al., 2007, 2008). Furthermore, our participants' EBR increased during the second block of transfer and during random trials. These data fit well with fMRI studies pointing out striatal modulations during blocks of transfer (e.g., Gobel, Parrish, & Reber, 2011; Seidler et al., 2005). Accordingly, the EBR time course and the transfer effect recorded in our study might be an indirect psychophysiological correlate of the dopaminergic activity occurring during a paradigmatic session of SRT.

EBR sensitivity to sequential irregularities could take some time to be evidenced and would necessitate additional learning blocks. In support of this interpretation, the trend for a higher transfer effect on RTs during the second block would advocate for a deeper internalization of the sequential material at this stage of learning, in comparison to the first block of transfer. This hypothesis could be investigated with regard to the consolidation

processes at work during sequential learning (Albouy, King, Maquet, & Doyon, 2013; Doyon et al., 2009; King, Hoedlmoser, Hirschauer, Dolfen, & Albouy, 2017; Robertson, Pascual-Leone, & Miall, 2004). Indeed, a transfer effect on EBR might be more apparent after the sequential structure has started being consolidated following an off-line period of time such as a 30-min break (Mary et al., 2015; Schmitz et al., 2009) or a night of sleep (e.g., Borrigan, Urbain, Schmitz, Mary, & Peigneux, 2015; Urbain et al., 2013; for a review see King et al., 2017). Additionally, both the position of the random block in the SRT learning session and its intrinsic nature (random vs. unlearned, structured sequence) might jointly modulate EBR. Indeed, our data suggest that EBR-related changes in random trials differed from those associated with another sequence, but only when the random block was set in the second position. Overall, this suggests that EBR modulations might occur if the block of transfer is not structured and takes place only after a sufficient amount of practice has allowed the sequence to be learned. This hypothesis should be tested in an experimental design in which transfer blocks (random vs. structured) are administered at various pre-set times during the SRT training session.

EBR-related changes occurred only for random trials compared to an unlearned but structured material (i.e., another sequence), underlining the importance of the nature of the block of transfer. This result might be in line with neuroimaging studies showing a higher striatal activity for random compared to sequential material (e.g., Poldrack et al., 2005; Schendan et al., 2003). Interestingly, the RTs and EBR transfer effects were negatively correlated during random trials. More specifically, beyond a higher average EBR during random trials, participants who were the less slowed down during the random transfer effect were also those who had the highest increase in their EBR. This pattern of results might be explained according to the inverted-u-shaped dopaminergic response in tasks requiring cognitive control (Cools & D'Esposito, 2011; Jongkees & Colzato, 2016). According to this

model, too low levels of dopamine (i.e., lower EBR) induce perseverations and lack of flexibility face to novel cognitive processing, whereas increased dopaminergic levels (i.e., higher EBR) may prompt a better cognitive integration even if it can be associated with distractibility. Therefore, a global increase of EBR during the block of transfer might be the consequence of a shift in a more controlled mode in order to integrate and respond faster to the random trials that cannot be predicted anymore. At an inter-individual level, this may also explain why participants with an upsurge in their EBR were the fastest in the random block (i.e., a lower transfer effect). Interestingly, an alternative but not mutually exclusive hypothesis could be related to the fact that random trials in the present experiment were not controlled for reversals, namely that a spatial position could reappear in a second consecutive trial (e.g. 1-4-1). Indeed, reversals may prime attentional disruption during sequential learning and potentiate the transfer effects observed on EBR excepted when participants are faced to an unlearned but structured material (for a discussion on the impact of reversals see Vaquero et al., 2006). Given the importance of attentional processes in both sequence learning (Jimenez, 2003) and EBR (Jongkees & Colzato, 2016), the effective role of this parameter would deserve to be specifically investigated in future studies. Overall, these data emphasize the importance of recording EBR in a more “phasic” or event-related way (i.e., when participants are performing a task or when EBR recordings are tightly synchronized with each stimulus display). This latter method has been successfully applied to highlight real-time changes in the event-based EBR during working memory updating (Rac-Lubashevsky, Slagter, & Kessler, 2017). It would be tempting to apply this methodology to sequential learning given the close relationship between the SRT and working memory (e.g., Frensch & Miner, 1994; Guzman Munoz, 2018; Unsworth & Engle, 2005).

EBR in the first resting state session was correlated to the magnitude of the accuracy transfer effect. This result suggests that spontaneous inter-individual differences in

dopaminergic activity as indexed by resting EBR might predict ulterior sequential learning ability. This result fits with a fMRI study showing that striatal resting activity is predictive of performance in a variant of the probabilistic SRT (Stillman et al., 2013). The correlations observed in our study might be in line with the inverted-u-shaped model of dopaminergic activity related to cognitive control (Cools & D'Esposito, 2011; Jongkees & Colzato, 2016). According to this model, participants who spontaneously blinked more at rest might present higher distractibility, and therefore be more impaired when facing new information (e.g., a transfer block). Alternatively, high blinkers might be more successful to learn sequential regularities and thus be more impacted by the transfer blocks. This interpretation might be corroborated by the correlation observed between the first EBR resting session and the RTs slope, suggesting that high blinkers had a steeper learning curve. Moreover, resting EBR might be relevant to predict SRT transfer effect, but only when the sequential material is not sufficiently consolidated (first block of transfer) and/or when it has no internal structure (random block). It should also be noted that the higher EBR effect present in the first resting session as compared to the EBR recorded on-line advocates for a qualitative difference between them. Accordingly, EBR may depend on different cerebral dopaminergic processes as a function of the ongoing cognitive task. In line with this assumption, previous studies have showed that cognitive demands may affect the amount of EBR (e.g., Benvivoglio et al., 1997; Chen & Epps, 2014; Fukuda, 1994; Schafer & Fachner, 2015; for short reviews see Neumann & Lipp, 2002; Stern, Walrath, & Goldstein, 1984). Consequently, the EBR recorded in the second resting session might have been contaminated by the cognitive processes at work during the SRT. Additionally, the presence of a poorer consistency in resting EBR in the SOC1 group might have reduced the probability to observe an equivalence between the two EBR resting sessions in the whole group, and/or some EBR related effects in the SOC1 group (see Figures 3 and 5). Therefore, the absence of a previous cognitive demand and/or the

relatively good consistency of the first resting session might explain why the resting EBR was predictive of participants' performance when EBR was recorded before but not after the SRT.

Unexpectedly, participants exposed to the SOC2 during the SRT session were able to generate above chance level some triplets belonging to the learned but also to the reverse sequence. This suggests that participants had enough explicit knowledge of SOC2 to control their representation in order to carry out the Exclusion condition of the generation task (Destrebecqz & Cleeremans, 2001; Fu, Fu, & Dienes, 2008). A difference in the internal structure of our sequences could have primed an intentional learning mode in participants who had to learn the SOC2 and explain why they acquired more explicit knowledge. Several studies have indeed underlined the importance of sequence structure on the extent to which learning is explicit (Cohen et al., 1990; DeCoster & O'Mally, 2011; Reed & Johnson, 1994; Seger, 1997; Vaquero et al., 2006; Wilkinson & Shanks, 2004). Congruently with this assumption, some specific triplets of the SOC2 were generated more often than others in the Inclusion condition, compared to the relatively good homogeneity of the triplets generated in the SOC1 group (see Table B.1). Triplet 132 was the triplet the most often reproduced in the Inclusion condition. It should be noted that this triplet was the only one depending exclusively on the fingers of the left hand (461325142635), whereas another triplet depending on the fingers of the right hand was present in both SOC1 (531624152364) and SOC2 (461325142635). Finally, left- and right-hand triplets were contiguous in SOC2 (461325142635). Consequently, the structure of each sequence might explain the disparity of performance in the generation task. Previous studies have showed that intentional learning is generally associated with a higher transfer effect (Guzman Munoz, 2018; Miyawaki, 2006; Russeler & Rosler, 2000; Schendan et al., 2003; Unsworth & Engle, 2005). The persistence of significant EBR transfer effects in the SOC2 group might thus reflect a differential learning mode during sequence learning. This hypothesis could be tested in a protocol in which half of

participants would be explicitly told about the presence of sequential regularities before performing a SRT session, compared to the other half who would remain untaught (i.e., an intentional vs. incidental group, respectively). Furthermore, an additional consolidation effect cannot be excluded. Indeed, the internal structure of the SOC2 and the resulting intentional mode of learning might have boosted the consolidation of some chunks of the sequence (King et al., 2017; see above), and increase the probability to observe EBR-related effects. An experimental paradigm allowing an off-line period of time between the two SRT sessions would allow to test more clearly this assumption.

The lack of relationship between EBR and performance in the generation task was unexpected, given that a ^{11}C -raclopride PET scan study previously showed that generation scores following a deterministic SRT learning session were associated to spontaneous D2 dopaminergic activity during resting state (Karabanov et al., 2010). In that study, participants were not taught about the presence of sequential regularities (i.e., incidental learning), and exhibited both implicit and explicit knowledge in the generation task. Our study differs in several respects. The pattern of performance in the generation task evidenced in the previous study seems to be very similar to the one observed in the SOC2 group, whereas the SOC1 group performed at chance level in the Exclusion condition. However, participants might have learned the SOC2 according to an intentional mode triggered by the internal structure of the sequence. Therefore, half of our participants (SOC2) could have intentionally learned the sequence, while the other half (SOC1) incidentally learned the sequence and failed to demonstrate any explicit knowledge when they had to generate backward the learned sequence. It should also be noted that the instructions of the Exclusion condition differed from Karabanov et al. (2010). Our participants had to generate the reverse sequence instead of simply avoiding generating the learned sequence. These methodological differences might explain why resting EBR does not appear to predict the degree of implicit or explicit

knowledge in our study. Further studies should more carefully investigate each of these parameters. Additionally, it should be interesting to record the EBR when participants are performing the generation task. An online measure might be more sensitive and/or relevant.

An interesting extension to the present study would be to use alternative versions of the deterministic SRT, namely the probabilistic SRT (Cleeremans & McClelland, 1991) or the ASRT (Howard & Howard, 1997). These versions would have the advantage to reduce drastically the amount of explicit knowledge of the hidden sequential material and, therefore, minimize the risk of becoming aware of some regularities during the learning session. Indeed, our data suggest that both awareness and explicit knowledge might have an impact on the relationship between EBR and SRT performance. It should be noted that these factors might also account for a weaker inter-session reliability in the transfer effect observed in the deterministic SRT (Stark-Inbar, Raza, Taylor, & Ivry, 2016; West, Vadillo, Shanks, & Hulme, 2018), whereas the ASRT evidenced a good consistency of the gradual differentiation between the structured and random trials over two separate learning sessions (Stark-Inbar et al. 2017). In addition to reduce the degree of awareness and explicit knowledge, the progressive measure of sequential learning all along the session of the probabilistic versions of the SRT might also indirectly fix some putative interindividual, fluctuating factors such as transient boredom or intrinsic motivation (Stark-Inbar et al. 2017; West et al., 2018). Further studies using the different versions of the SRT will be useful to carefully investigate the respective effect of each of these parameters and extend the current data. Within this framework, the present protocol could be applied to some specific populations known for their abnormal dopaminergic activity and their impairment during sequential learning, such as normal aging (Schuck et al., 2013), Parkinson's disease (Clark et al., 2014; Ruitenberg et al., 2015; Siegert et al., 2006), or schizophrenia (Remillard, 2014; Siegert et al., 2008).

5. Conclusion

The present study shows, for the first time, that EBR is sensitive to sequential learning and to the presence of deviations from a learned sequence. Participants performing a SRT exhibit gradual changes in their accuracy and RTs in parallel to the time course of EBR. EBR-related changes are essentially evidenced when the block of transfer is composed of random trials and occurs at the end of a learning session, suggesting the relative importance of the nature and the position of the block transfer during sequential learning. Behavioral (RTs) and psychophysiological (EBR) markers were negatively correlated during random trials. In addition, accuracy during the first block of transfer and random trials was predicted by inter-individual difference in resting EBR. A better cognitive integration of a novel material in participants who demonstrated higher EBR might explain these results. Overall, our data suggest that the EBR recorded online is a relevant index of dopaminergic activity related to sequential learning, in addition to resting EBR. Subsequent studies using of the probabilistic versions of the SRT might better control for unpredictable factors and probe the generalization of the dopamine-related effects evidenced in the present study. Additionally, this experimental protocol might be applied to normal aging, parkinsonian or schizophrenic patients given the atypical dopaminergic activity within these specific populations during sequential learning.

Conflicts of interest

The authors declare no conflict of interest in this work.

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Appendix A

Table A.1 – One-tailed Sample T-Test against 0 for each transfer effect according to the learned SOC

Transfer Effect ($B_N - B_{N-1}$)			Mean (SD)	t	<i>p</i>	Cohen's <i>d</i>	BF_{10}
SOC1 (n = 16)	Accuracy (%)	TSF1	-3.65 (3.71)	-3.93	< .001	.98	59.93
		TSF2	-3.06 (3.91)	-3.13	0.003	.78	14.91
		RAND	-4.43 (3.41)	-5.19	< .001	1.30	524
		SOCb	-2.28 (3.88)	-2.35	0.017	.59	4.07
	RTs (ms)	TSF1	97 (70)	5.55	< .001	1.39	963
		TSF2	109 (68)	6.34	< .001	1.58	3.41*10 ³
		RAND	120 (64)	7.47	< .001	1.87	1.90*10 ⁴
		SOCb	86 (70)	4.89	< .001	1.2	313
	EBR (EB/min)	TSF1	-.04 (3.9)	-0.04	.52	.01	.25
		TSF2	.69 (3.4)	0.81	.22	.20	.53
		RAND	.64 (3.4)	0.76	.23	.19	.50
		SOCb	.01 (3.9)	0.01	.50	.01	.26
SOC2 (n = 17)	Accuracy (%)	TSF1	-4.11 (4.27)	-3.98	< .001	.96	70.26
		TSF2	-5.83 (4.22)	-5.69	< .001	1.38	1.51*10 ³
		RAND	-6.01 (4.83)	-5.13	< .001	1.25	567
		SOCb	-3.93 (3.46)	-4.68	< .001	1.14	253
	RTs (ms)	TSF1	112 (50)	9.23	< .001	2.24	3.44*10 ⁵
		TSF2	139 (66)	8.71	< .001	2.11	1.69*10 ⁵
		RAND	147 (67)	8.99	< .001	2.18	2.49*10 ⁵
		SOCb	105 (42)	10.16	< .001	2.46	1.16*10 ⁶
	EBR (EB/min)	TSF1	.38 (2.7)	.57	.29	.14	.40
		TSF2	2.55 (3.8)	2.79	.007	.68	8.57
		RAND	2.46 (4.3)	2.37	.015	.57	4.22
		SOCb	.47 (1.9)	1.00	.17	.24	.63

Note: The alternative hypothesis specifies the mean is either less (Accuracy) or more (RTs and EBR) than 0

Appendix B

Table B.1. Average number of triplets generated in the Inclusion and Exclusion conditions according to each SOC

INCLUSION				EXCLUSION			
SOC1 (n = 16)		SOC2 (n = 17)		SOC1 (n = 16)		SOC2 (n = 17)	
Triplet	Mean (SD)	Triplet	Mean (SD)	Triplet	Mean (SD)	Triplet	Mean (SD)
513	2.27 (3.03)	461	4.89 (3.56)	354	.87 (1.81)	645	1.78 (2.65)
316	2.33 (2.55)	613	5.56 (3.97) ^a	546	.87 (1.85)	453	1.56 (2.59)
162	2.87 (3.78)	132	6.61 (4.19) ^b	463	1.87 (2.33)	536	1.39 (2.5)
624	2.13 (2.99)	325	4.72 (3.95)	632	1.4 (1.81)	362	1.44 (2.73)
241	1.47 (1.96)	251	3.78 (3.64)	325	1 (1.25)	624	1.39 (2.55)
415	1.67 (1.88)	541	3.17 (3.47)	251	1.07 (1.22)	241	2.89 (4.32)
152	2.47 (2.47)	142	2.89 (3.43)	514	1.53 (1.81)	415	3.06 (2.98)
523	2.47 (2.26)	426	2.72 (3.25)	142	1.47 (1.64)	152	4 (3.43)
236	2.4 (2.77)	263	2.67 (3.22)	426	1.87 (2.75)	523	3.17 (2.92)
364	2.33 (2.85)	635	2.94 (3.29)	261	1 (1.46)	231	3.39 (3.36)
645	3.13 (3.44)	354	3.28 (3.18)	613	1.53 (2.36)	316	3.28 (3.32)
453	2.13 (3.38)	546	3.89 (3.36)	135	2.2 (3.09)	164	1.83 (2.71)

Note: Bonferroni posthocs: (a) different from the 8th and 9th triplets, $ps < .05$; (b) different from the 5th to 11th triplet, $.001 < ps < .05$

Appendix C

Table C.1. Correlational analyses between the different variables associated to the transfer effect (accuracy, RTs and EBR) according to the nature of the block of transfer (random vs. new sequence, SOCb), and with eyeblinks recorded during the two resting states, for all participants and the SOC1 and SOC2 groups

		EYEBLINKS											
		ALL PARTICIPANTS (n = 33)				SOC1 (n = 16)				SOC2 (n = 17)			
		TSF1	TSF2	RES T1	RES T2	TSF1	TSF2	RES T1	RES T2	TSF1	TSF2	RES T1	RES T2
ACCURACY	TSF1	-.37*	.12	-.42*	-.21	-.53*	.15	-.19	-.16	-.21	.15	-.55*	-.25
	TSF2	-.24	-.09	-.29	-.07	-.36	.07	-.06	.29	-.10	-.07	-.29	-.27
REACTION TIMES	TSF1	-.21	.02	-.01	-.01	-.27	.11	-.12	-.21	-.11	-.16	.01	.18
	TSF2	-.29	-.17	-.09	-.19	-.26	.05	-.06	-.30	-.41	-.50*	-.26	-.16
EYEBLINKS	TSF1	-	.29	.03	-.02	-	.26	-.06	-.09	-	.34	-.04	.17
	TSF2		-	-.08	-.02		-	.02	-.11		-	-.17	-.09
	RES T1			-	.53*			-	.37			-	.61*
		Random	SO Cb	RES T1	RES T2	Random	SO Cb	RES T1	RES T2	Random	SO Cb	RES T1	RES T2
ACCURACY	Random	-.22	-.07	-.43*	-.24	-.33	-.08	.14	.01	-.11	-.04	.61*	-.36
	SO Cb	-.11	-.14	-.29	-.03	-.26	-.13	-.38	.13	.09	-.17	-.18	-.14
REACTION TIMES	Random	-.43*	.09	-.07	-.16	-.46	.19	.01	-.20	-.54*	-.10	-.24	-.16
	SO Cb	-.35*	.15	-.03	-.05	-.43	.17	-.19	-.32	-.43	.06	-.01	.23
EYEBLINKS	Random	-	.29	-.01	.09	-	.26	-.13	.17	-	.41	-.08	.03
	SO Cb		-	-.03	-.18		-	.07	-.33		-	-.23	-.02

Note: (*) $p < .05$, (**) $p < .01$, (***) $p < .001$, Bold: $BF_{10} > 3$