A Study on Event-Related Potentials during Decision-Making in a Mix-Strategy Game

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論　文　内　容　要　旨（和文）

学位論文題名	A study on event-related potentials during decision-making in a mix-strategy game ゲーム理論を応用した意思決定課題による事象関連電位の研究

運動準備電位は運動遂行に先行して出現し徐々に増大する陰性電位でその振幅は効果器や準備する運動の種類、運動開始が自発性か外部刺激によるかなどに依存して変化する。パーキンソン病では運動準備電位が低下し l-DOPA 治療で回復することから、運動準備電位の生成にはドパミンが関与していると考えられる。本研究では意思決定過程が運動準備電位に及ぼす影響を検討するために、マッチングペニー課題と呼ばれるゲーム理論を応用した意思決定課題を用いて l-dopa またはプラセボ投与下で脳波記録を行った。被験者はコンピューターモニターに向かい合って座り、画面に提示された左右のターゲットをキーボードのキーを押して選択する。被験者が選択を行った後に対戦相手のコンピューターが選択を行った。対戦相手の選択と自己の選択が一致すれば被験者が勝ち、不一致であればコンピューターが勝つというルールを設定した。GAME 条件ではコンピューターは被験者の過去の選択パターンを分析して次試行での被験者の選択行動を予測し、その予測と反対のターゲットを選択するようプログラムされた。GAME 課題の対照実験として対戦相手が左右方向を交互に選択する ALT 条件と左右方向を無作為に選択する RAND 条件を行った。GAME 条件では被験者は過去の対戦相手の選択と同じ方向を選択する傾向がみられ、RAND 条件では被験者自らの１試行前の選択と反対側を選択する傾向がみられた。脳波の解析の結果、行動選択に先行して正中頭頂部に持続的な陰性電位が観察され、GAME、RAND、ALT の３条件の間で有意差はみられず、l-dopa 投与でも変化しなかった。この運動に先行する持続陰性電位は過去に運動準備電位として報告された電位に相当すると考えられた。また、運動遂行後に対戦相手の選択が呈示され勝敗結果が示される時間帯に陰性から陽性にふれる二相性電位が観察された。この電位は GAME、RAND 条件において ALT 条件より有意に大きく、l-dopa 投与によって陰性側にシフトした。フィードバック情報に随伴してみられるこの電位は古典的に contingent negative variation (CNV)と呼ばれる誘発電位に類似のものと考えられた。以上より、運動準備電位は健常人では認知過程や l-dopa の影響が小さく、CNV 様電位は意思決定過程と l-dopa の影響を受けやすい電位と考えられた。

（Clinical Neurophysiology）

1. Introduction

Event-related potentials (ERPs) are averaged amplitude fluctuations of the ongoing electroencephalographic (EEG) activity that are time locked to certain sensory, motor or cognitive events (Georgiev, Lange, Seer, Kopp, & Jahanshahi, 2016). The ERPs can be evoked by either external stimuli or internal mental processes. Movement-related potentials (MRPs) are special types of the ERPs associated with processes of voluntary movement preparation, initiation, or execution (Georgiev et al., 2016). The early component of the MRPs is also called the Bereitschaftspotential (BP), which slowly increases its negative potential 1 to 2 seconds before movement execution (Cunnington, Iansek, Bradshaw, & Phillips, 1995). Previous studies suggested involvement of the dopamine system in the BP. The amplitude of the BP was smaller in Parkinson's disease (PD) patients than healthy controls, and the reduced amplitude of BP was restored by dopaminergic therapy (Amabile et al., 1986; Oishi, Mochizuki, Du, & Takasu, 1995). The source of dopaminergic influence on the BP may be the mesolimbic cortical projection to the supplementary motor area, which is thought to be the generator of the BP.

Movement preparation may either be simple motor processes or more complex processes involving cognitive components such as decision making. For example, alternating key pressing between two keys requires preparation of a simple motor sequence, and playing lock-paper-scissors involves more complex interactive decision processes. Decision is a deliberate process that results in the commitment to a categorical proposition (Gold & Shadlen, 2007). Level of decision-making changes depending of decision variables such as likelihoods, priors, and values. In most studies, simple finger movements, such as index finger extension or thumb opposition, have been used for eliciting the MRPs. However, it is unknown how the MRPs are affected by complex decision-making.

In this study, we aimed to control for the level of cognitive load and choice flexibility by using a binary choice task. To require highly cognitive and flexible decision-making, we used a matching pennies task, which is a type of mixed strategy zero-sum game, like lock-paper-scissors, based on a given pay-off matrix (Table 1). We hypothesized that higher cognitive load and choice flexibility and l-dopa treatment both cause enhancement of the MRPs amplitude.

2. Methods

2.1 Subjects

Eighteen right handed healthy adults (male: 12, mean age 46.2±12.8 years old) were recruited in the current study. One male subject was excluded because he withdrew from the experiment after the first session. Fukushima Medical University ethical committee had approved the experimental design of the study. Informed consent was obtained from all the subjects.

2.2 Procedures

Each subject participated in the recordings two times with at least a week of interval. Subjects took either placebo or 100mg l-dopa 45 minutes before the start of each recording. Drug treatment was double-blinded and randomized.

During EEG recording, the subject was seated in front of a computer monitor (60cm× 30cm) at 70cm distance. The subject played a computerized version of the matching pennies task (Fig. 1). At the beginning of each trial, two grey circles were displayed at the bottom of the monitor and the subject put the index and middle fingers of the right hand on the two designated keys on the keyboard (WAIT period). After 800 ms, the grey circles changed color, which signaled the subject to press either one of the two keys (GO period). Immediately after the choice, a hand illustration was displayed below the chosen side of the circles (SBJ Choice). After 1,000 ms, the choice of the opposing PC player was revealed by a hand illustration shown on the left or right side of the top of the display (OPP CHOICE). If the side of the choice matched or nonmatched between the subject and the opposing PC player, the subject won or lost the trial, respectively. After 700 ms, the outcome of each trial was displayed together with the total winning rate on the screen (FEEDBACK). The subject was encouraged to win as much as possible. If the subject responded during WAIT period, the trial was aborted. If the subject did not respond within 5 seconds after GO signal, the trial was aborted.

Algorithms for the opposing PC player: Each subject performed the matching pennies task with three different rules. In the alternation (ALT) rule, the opposing PC player chose the left or target alternatively. Therefore, the subject could predict the opponent's choice easily in ALT rule. In the random (RAND) rule, the opposing PC player chose the left or right target randomly at equal probability. Therefore, the subject could not predict the opponent's choice. In GAME rule, modified from a previous study (Barraclough, Conroy, & Lee, 2004), the computer exploited any systematic bias in the subject's choice and win/lose outcome in the recent past to maximize the PC player's winning rates. The computer saved the entire history of the subject's choices in a given session, and used the information to predict the subject's next choice by testing a set of hypotheses. The conditional probabilities of choosing each target given the subject's choices in the preceding n trials (n= 1 to 4) were estimated. The computer biased its selection according to the probability with the largest deviation from 0.5. For example, if the subject chose the right-hand target with 80% probability in the recent past, the computer selected the left-hand target with 80% probability. Also, for example, if the subject chose the right-hand target with 80% probability after losing a trial by choosing the left-hand target (lose switch strategy), the computer selected the left-hand target with the same probability. Therefore, to maximize the chance of winning, the subject needed to choose both targets with equal frequency and select a target on each trial independently from previous choices.

All subjects played 450 trials (6 sessions with different rules, 75 trials/session). Six sessions were run in a fixed order (ALT, RAND, GAME, ALT, RAND, GAME) and there was a short break between the sessions. We also instructed to look at the cross mark at the center of the monitor to avoid eye movement. At the beginning of the experiment, the task procedure and the three different rules of the opposing player were instructed and the subjects underwent a practice session of 15 trials. Furthermore, the relevant rule was explicitly instructed to the subjects when a new session began. The behavioral task was controlled by MATLAB 2012 (The MathWorks, Inc., Natick, Massachusetts, United States) with Cogent2000 and the Psychophysics Toolbox (Brainard, 1997) running on a Windows computer connected with a Macintosh computer that sampled EEG data.

2.3 Data acquisition and analysis

We analyzed the subjects' winning rates in each rule. We evaluated how much the subject's choice was influenced by the subject's own choice in the past by using log likelihood (LR),

$$LR_{self}(n) = \log[\{p(rt_{self},rt_{self}) + p(lt_{self},lt_{self})\}/\{p(rt_{self},lt_{self})+p(lt_{self},rt_{self})\}] \quad (1)$$

where $LR_{self}(n)$ is the LR of choosing the same side in the current trial as in n trials before, and $p(A_{self}, B_{self})$ is the conditional probability of the subject to choose A in the current trial and to choose B in n trials before. If there is no influence from the past choice, $LR_{self}(n) = 0$. If the subject tends to choose the same side as or the opposite side from the choice in n trials before, $LR_{self}(n)$ would be positive or negative, respectively.

The subject's current choice could also be influenced by the opponent choice in the previous trials. The influence from the past choice of the opposing PC player was evaluated in an analogous way,

$$LR_{pc}(n) = \log[\{p(rt_{self},rt_{pc}) + p(lt_{self},lt_{pc})\}/\{p(rt_{self},lt_{pc})+p(lt_{self},rt_{pc})\}] \quad (2)$$

where, $LR_{pc}(n)$ is the LR of choosing the same side in the current trial as the opponent's choice in n trials before, and $p(A_{self}, B_{pc})$ is the conditional probability of the subject to choose A in the current trial when the opposing PC player chose B in n trials before.

Electroencephalography (EEG) data were recorded from 129 scalp locations at the sampling rate of 1000 Hz with a 24-bit A/D conversion. (Geodesic EEG System 400, Electrical Geodesic Inc., USA). EEG data analysis was performed using EEGLAB 14.1.1(Delorme & Makeig, 2004) and ERPLAB 6.1.4 (Lopez-Calderon & Luck, 2014) running under MATLAB R2014a (The MathWorks, Inc., Natick, Massachusetts, United States). The data were downsampled to 250 Hz, high-pass filtered at 0.01 Hz, low-pass filtered at 30 Hz, and notch filtered at 50 Hz. Bad channels were removed and the removed channels were interpolated. The sampled data were re-referenced to the average of all electrodes. Independent Components Analysis (ICA) and ADJUST (Mognon, Jovicich, Bruzzone, & Buiatti, 2011) were used to correct artifacts such as blinks and eye movements. ERPs in the three periods were analyzed (Fig. 4). The first period (Ⅰ) was from the onset of WAIT cue until the onset of GO cue. The second period (Ⅱ) was -800ms to 0ms from the subject choice response (SBJ CHOICE). The third period (Ⅲ) was from the disclosure of the opponent choice (OPP CHOICE) until the onset of feedback cue (FEEDBACK). The activity during the inter-trial interval was used for the baseline correction. We excluded EEG data with large proportion of noise contamination (over 25% of trials rejected by ERPLAB). Data from seven subjects were excluded in this study.

2.4 Statistical analysis

2.4.1 Behavioral data

Rates of winning were analyzed for each subject for each rule. Average winning rates were subjected to 2-way ANOVA (drug, l-dopa; placebo) × (rule, RAND; GAME). Behavioral data from the ALT condition were not included because subjects won almost 100% of trials. We tested whether $LR_{self}(n)$ and $LR_{PC}(n)$ were significantly different from 0 by 2-tailed t-test. Significance level was set at 0.05 with multiple comparisons corrected by the Bonferroni method. The analysis was done using statistics toolbox of MATLAB.

2.4.2 Electrophysiological data

The effects of l-dopa and rule on the ERPs were tested by two-way repeated ANOVA (drug, l-dopa; placebo) × (rule, ALT; RAND; GAME) using SPSS statistical software (IBM, version 23, Armonk, New York). Significance level was set at 0.05 with multiple comparisons corrected with Tukey HSD.

3. Results

3.1 Behavioral results

We included the data from all subjects for behavioral analysis (Fig. 2A). Two-way repeated ANOVA revealed a significant main effect of rule ($p<0.05$), but the main effect of l-dopa treatment and interaction effect were not significant. Post-hoc test specified that winning rate in ALT was higher than the wining rate in RAND or GAME ($p<0.05$). Wining rate in RAND was significantly higher than wining rate in GAME ($p<0.05$).

In GAME sessions, the subjects could play better by choosing targets independently in each trial because any choice bias could have been exploited by the computer. We evaluated how much the subjects' choice was dependent on their own choices in the past by using log likelihood ratio (LR) method (Fig. 3). Influences from the past choice of the subject (n trials before) are expressed as the $LR_{self}(n)$ (Fig. 3A). The $LR_{self}(1)$ was significantly negative in RAND sessions with l-dopa, indicating that subjects tended to choose the target opposite to the one they chose in a trial before. There was no significant past influence in GAME sessions. In the similar way, we analyzed the influences of the opponent's past choices (Fig 3B). The $LR_{PC}(n)$ was significantly positive in GAME sessions for $n \geqq 2$ independent of l-

dopa treatment, indicating that the subjects tended to choose the target on the same side as the target chosen by the opposing PC player in the past.

3.2 Electrophysiological results

We averaged EEG activity recorded with the Cz electrode and aligned it to the start of trials (WAIT) and subject's choice response (SBJ CHOICE). The activity is plotted separately for the three different task rules with and without l-dopa (Fig. 4). In this study, we focus on two distinct potentials, namely the sustained negative potential during motor preparation period (periods II and III) and the biphasic potential observed around the time of the opponent choice (period III). After phasic response to the WAIT cue, we observed sustained negativity throughout the periods II and III. The activity went back to the baseline after the subject made the key press response. The negativity was distributed around the mid frontal region. During period III, when the opposing player's choice was exhibited on the screen, the negative potential built up again, which made an abrupt deflection toward positivity and went back to the baseline after the outcome feedback was provided on the screen. The negative peak was greater in RAND and GAME rules as compared with ALT rule and it was distributed at the mid frontal region.

Table 2 summarizes the amplitudes of ERPs. During the periods I and II, there was no significant effect of rule or treatment. During the period III, the ERPs showed negative-to-positive biphasic peaks and ANOVA was performed for the amplitude of each peak. For both peaks, the drug main effect was significant ($p<0.05$), indicating that l-dopa enhanced the ERP amplitudes. The main effect of rule was also significant in period III ($p<0.05$), indicating that the ERP amplitudes were larger in the RAND and GAME sessions as compared with ALT sessions. There was no significant interaction between drug and rule.

In RAND and GAME sessions, behavioral winning rates were approximately 50%. Trials in which the subjects won and lost against the opposing PC player are merged in Fig. 4. To examine whether the ERPs differentiated the choice outcome, we averaged the ERPs separately for each outcome (Fig. 5). Although there was a tendency that ERPs in winning trials were more negative than those in losing trials during GAME condition with l-dopa medication, three-way ANOVA (rule [ALT, RAND, GAME]×drug [l-dopa, placebo]×outcome [win, lose]) revealed no significant main effect or interactions ($P>0.05$). Thus, the ERPs did not differentiate the decision outcome.

4. Discussion

We aimed to study whether ERPs reflect decision process during performance of a binary choice task. We found that behavioral performance changed according to the decision rules for left-right target choice, which confirms that subjects understood the instructed rules and adapted their choice behavior according to the rule. Behavioral performance in ALT sessions was nearly perfect, as expected, reflecting the easiness to predict the opponent choice. By contrast, behavioral performance in RAND was close to the chance level, as we intended. Interestingly, behavioral performance in GAME was slightly but significantly lower than that in RAND. This indicates that subjects made partially predictable choices, and consequently they were exploited by the computer player to some extent. This point is supported by the analysis on behavioral history effects; subjects tended to choose the same side of the target as the computer chose in the past (Fig. 2B).

We did not find significant effect of l-dopa on the behavioral performance in sessions of any rule. Previous studies that reported the influence of l-dopa on decision-making were often driven by reward incentive (Chowdhury et al., 2013). Thus, it is possible that cognitive decision-making without salient reward drive may be less sensitive to dopaminergic treatment. In sum, behavioral analyses revealed that decision process changes dynamically and past choices have different influences on the present choice adapting to different task rules.

We found two different types of ERPs during the performance of our task. First, negative potential emerged after the signal of task start and it was sustained until subjects made choice responses. The sustained negativity is associated with movement preparation. Thus, the ERP appears to correspond to readiness potential or BP. The present behavioral task had several differences from the tasks conventionally used to study readiness potentials. First, in most of the previous studies, movements were self-paced and self-initiated. It has been known that readiness potential becomes weaker with an external trigger (Cunnington et al. Brain 1995). Our task had two external stimuli that signaled start of a trial: WAIT cue and GO cue. The phasic activity just after the WAIT cue appears to have been driven by the external stimulus, which might have deformed the waveform of BP in our study. Nevertheless, the activity preceding to the choice response has several signatures of BP, including sustained nature of negative activity and mid vertex topography. Second, our task was a decision task, which involves more cognitive processes than simple motor tasks used in conventional readiness potential studies. We hypothesized that different levels of cognitive load in decision process would change the size of readiness potential. The three rules in our task provided different

levels of cognitive load. However, against our hypothesis, the ERPs preceding to motor response did not change significantly by the rule. The result suggests that the observed ERP is reflecting down-stream motor process more than up-stream cognitive decision process.

We found that the effect of l-dopa was not significant. Previously, several studies reported increases of MRPs by l-dopa treatment in PD patients (Dick et al. 1989; Feve et al. 1992; Oishi et al. 1995), but the result was not consistent in another study (Barrett et al. 1986). The effect of l-dopa has not been studied in healthy subjects. Lack of l-dopa effect on MRPs in the present study might be because normal subjects are not deficient of dopamine. Another possibility is the dose of l-dopa. In the present study, we used 100mg l-dopa/10mg dopa-decarboxylase (DCI), which is a smaller dose compared to some of the previous studies. Dick and colleagues used 250mg l-dopa/25mg DCI, and Oishi and colleagues injected l-dopa 0.25% 20ml. Future study is needed to examine the l-dopa effect on the MRP in normal subjects.

The second type of ERP was observed between the events of the opposing player's choice and the outcome feedback. Negative potential built up after the disclosure of the opposing player's choice, which made a sharp deflection toward positivity and came back to the baseline just before the outcome feedback. This ERP was prominent during the GAME and RAND sessions and much smaller during the ALT session. The potential may be classified as contingent negative variation (CNV), which is a type of ERPs elicited between two contingent events with or without motor responses (Brunia, 2003). The two events of OPP CHOICE and FEEDBACK were temporally contingent with fixed interval of 700ms. The event contents were also contingent because provided the information of the opposing PC player's choice, the win/lose outcome was uniquely determined hence 100% predictable. Topography of the ERP was also similar to that of CNV with predominantly frontocentral distribution (Hamano et al., 1997). Previous studies reported that CNV of PD patients are reduced in amplitude as compared with that of healthy controls (Botzel et al. 1995; Cunnington et al. 2001; Gerschlager et al. 1999; Ikeda et al. 1997; Oishi et al. 1995; Wright et al. 1993), suggesting that there is a positive relationship between CNS dopamine level and CNV amplitude. L-dopa sensitivity of the CNV-like potential in the present study is consistent with the previous reports. The present study further suggests that the CNV-like potential is more sensitive to l-dopa than the MRP.

We also found that the amplitude of the CNV-like potential was greater during the RAND and GAME sessions as compared with the ALT sessions. The result is explained by information value of the feedback stimulus. The choice of the opponent player was not

predictable during the RAND and GAME sessions, thus the cue stimuli presented at OPP CHOICE and FEEDBACK were informative. However, during the ALT sessions, the alternating choice of the computer was highly predictable and the outcome was almost always win. Thus, the feedback was least informative. We found that negativity of the CNV-like potential increased by both l-dopa treatment and greater information value of the feedback stimulus. This is interesting considering that the dopamine system underlies reinforcement learning. Although we found the activity did not differentiate between positive versus negative outcomes, it may well be reflecting feedback learning processes, such as allocation of attention resource to the feedback.

In conclusion, the present study demonstrated the l-dopa-insensitive MRP preceding the binary choice and the l-dopa-sensitive and rule-selective CNV-like potential associated with feedback stimuli. An interesting future direction is to study how PD patients play the matching task and whether the ERPs are different from those from healthy subjects. It is also a fundamental question whether behavior and ERPs of PD patients are influenced by l-dopa in the matching pennies task.

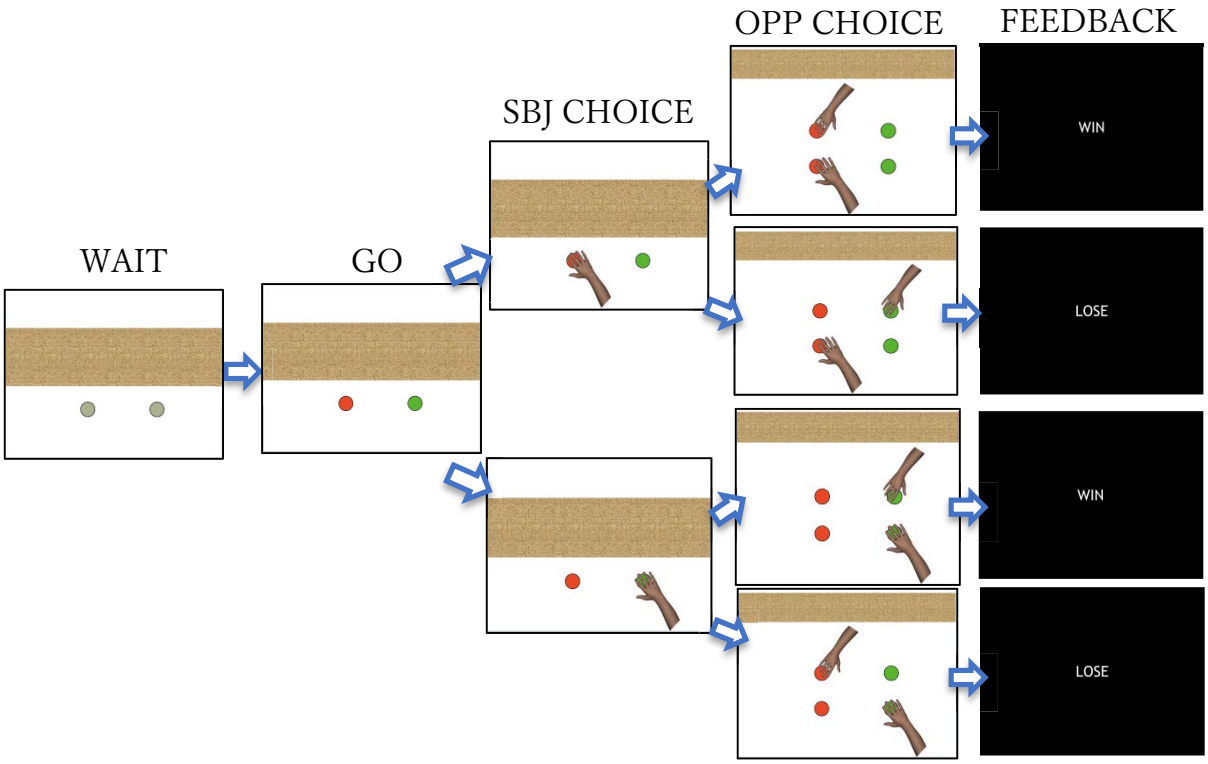

Fig 1. The matching pennies task

Illustration of the task flow. The task started with the presentation of the two grey circles (WAIT). Color change of the two circles signaled to make a choice response (GO). The subjects had to choose either left or right target (SBJ Choice). After 1000 ms delay, the opposing PC player was disclosed (OPP Choice). After 700 ms, the outcome was shown (FEEDBACK).

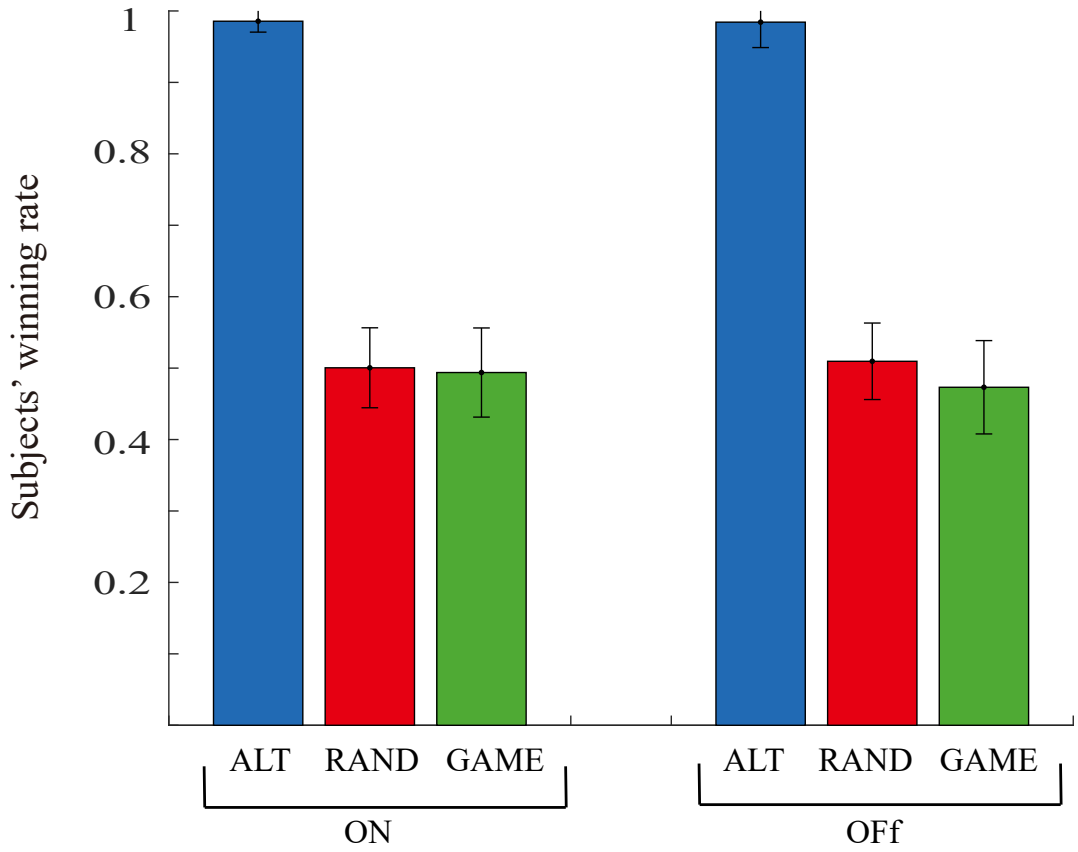

Fig. 2 Average winning rates in sessions with three different rules (mean±SD).
Two-way repeated ANOVA (rule×drug) revealed a significant main effect of rule ($p<0.05$). Post-hoc test specified that winning rate in ALT was higher than in RAND and GAME and winning rate in RAND was higher than GAME ($p<0.05$). There was no significant main effect of drug or interaction effect.

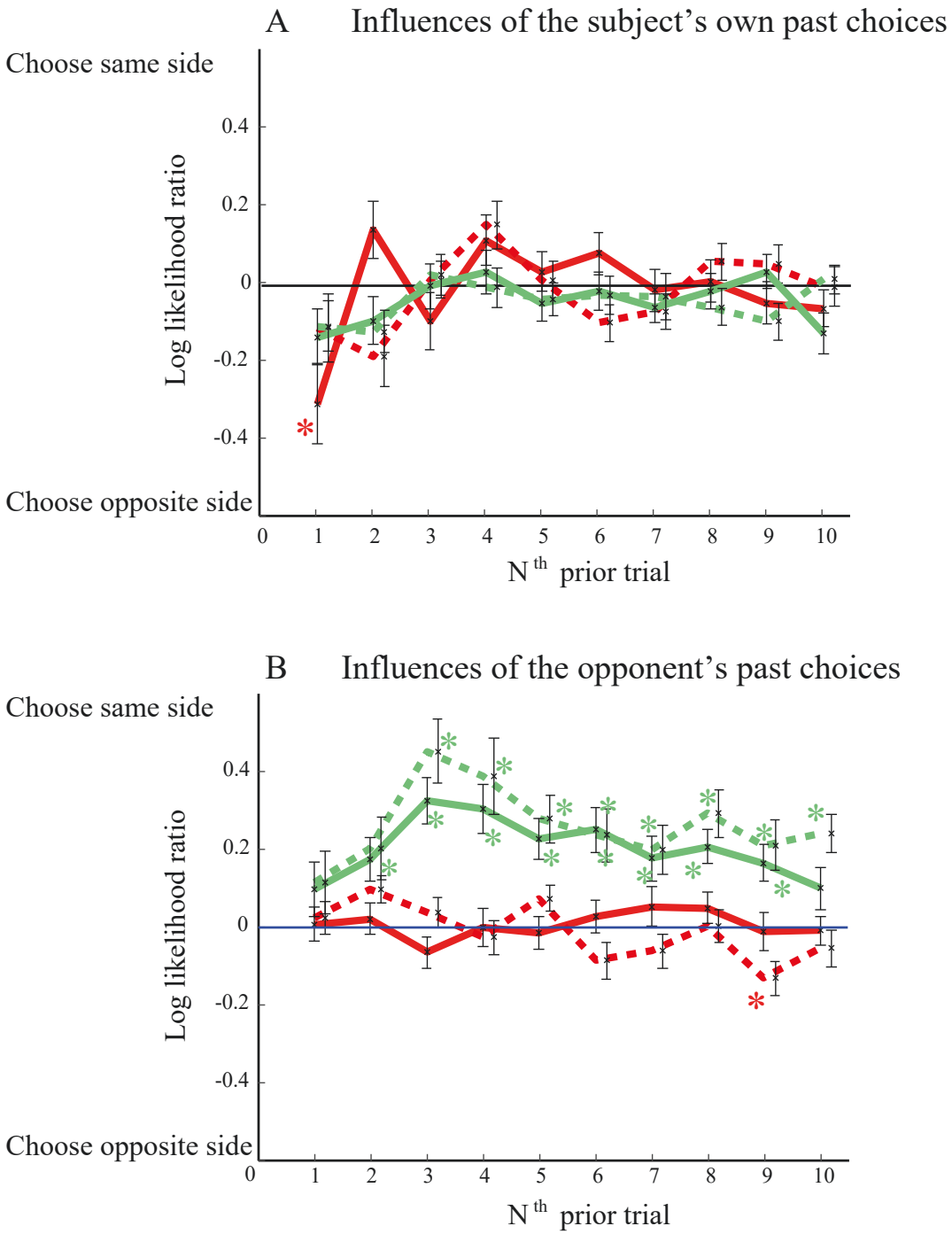

Fig. 3 The effects of previous choices on decision-making

The figure shows the influences of the past choices on the present choice by log likelihood ratio (LR, y axis) as a function of N^{th} prior trial (x-axis). Positive and negative LRs mean that the subject tended to choose the same side as and opposite side from the previous trials, respectively. (A) Influences from the subjects' own past choices. (B) Influences from the opposing player's past choices. Red lines, RAND rule; green lines, GAME rule. Solid lines, sessions with l-dopa; dotted lines, sessions without l-dopa. * indicates significant deviation from zero ($p<0.05$, student t-test).

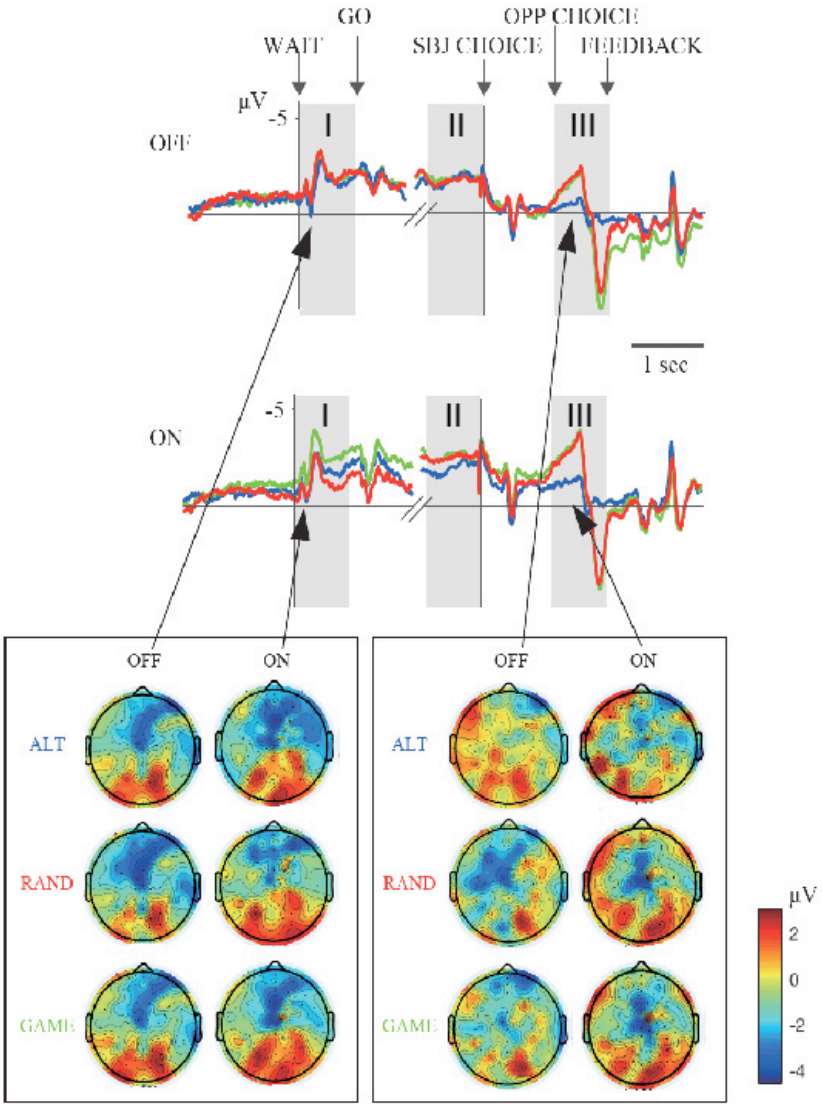

Fig. 4 ERPs in three different rules (blue, ALT; red, RAND; green, GAME). Gray squares (I, II, and III) indicate time windows for ERP analysis (cf. Table 2). Topoplots visualize amplitude distribution of the negative peak in period I and negative peak in period III.

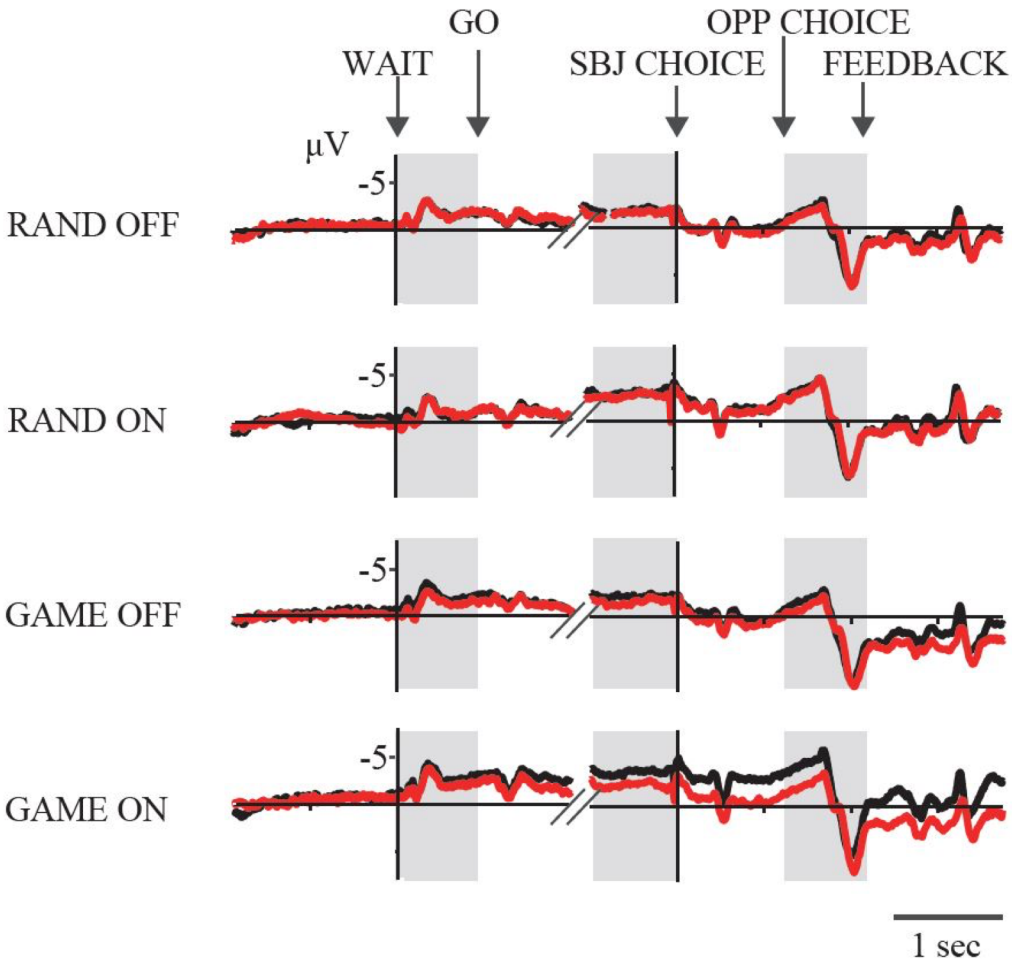

Fig. 5 The ERPs are plotted separately for trials in which subjects won and lost. Vertical lines indicate the onset of WAIT cue (left) and the subject's response (right). There was no significant main effects or interaction by 2-way ANOVA (rule ×drug) in all three task periods. Black line, trials in which subjects won; red line, trials in which trials lost.

Table 1. Pay-off matrix.

		PC's choice	
		Left	Right
Subject's choice	Left	[win, lose]	[lose, win]
	Right	[lose, win]	[win, lose]

The table indicates pay-off matrix of the subject and the opposing PC player for the choice of left versus right key press. [subject, PC]

Table 2. ERPs during the binary choice task. Averaged ERP amplitude is shown in three different rules during three task periods (mean±SD, μV; N=10)

Period	Rules	WAIT (Ⅰ)	Pre-response (Ⅱ)	FEEDBACK (Ⅲ)		
		Mean	Mean	Negative peak	Negative peak*	Positive peak♭
Placebo	ALT	-1.22±2.28	-1.66±2.74	-3.42±2.93	-1.19±1.81	2.52±1.58
	GAME	-1.60±2.82	-1.88±2.82	-2.95±2.67	-3.35±1.96	7.89±5.80
	RAND	-1.62±2.64	-1.66±2.75	-2.90±2.65	-3.57±2.42	6.87±4.82
L-dopa	ALT	-1.31±3.20	-2.04±3.58	-3.91±3.83	-2.41±1.08	1.70±0.87
	GAME	-2.23±2.86	-2.85±2.98	-4.03±2.92	-5.26±1.66	6.93±5.36
	RAND	-0.87±4.59	-2.70±2.83	-4.31±3.08	-5.05±2.85	6.20±3.86

*♭ Significant main effects for drug and rule by Two-way repeated ANOVA ($p < 0.05$). Post-hoc Turkey tests indicated that amplitudes in ALT and GAME were significantly more negative (*) and more positive (♭) than in ALT ($p<0.05$).

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