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The essential of applying nonlinear-analysis to validate experiments, assessing superior brain functions: Case-study of a Bayesian-Model of inhibitory control in ADHD

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Abstract

In the last decades, nonlinear methods have been applied, in a large number of studies from the computational neuroscience field, to describe neuronal implementations of superior brain functions. Superior brain functions, called cognitive functions, control our behavior. Therefore, they should be assessed by evaluating individual performances in the experiments, using standard tasks, which represent the condition that cognitive functions are required. The mathematical models of cognitive functions, at the neuronal implementation level, are based on the real condition of standard cognitive tasks. However, it is not validated whether applied task conditions are appropriate to represent the neuronal implementation of a cognitive function. Hence, as a case study, we used a developed Bayesian Model to assess whether the GoNoGo task is valid to be applied for neural measurement and modeling neural implementation of Inhibitory Control (IC). As GoNoGo is the most common task used for neural measurement of impaired cognitive function (IC) in ADHD, we fit the model to behavioral data of two groups of children/adolescents with and without ADHD. The results demonstrated that the model could simulate the behavioral data, and also the model parameters could differentiate the groups significantly. However, the neural implementation of IC may not be represented through the rewarded condition of the GoNoGo task. We concluded that before modeling the neural implementation of cognitive functions, it is essential to apply nonlinear methods to validate current behavioral experiments computationally; or to design new model-based experiments for use in neural measurements.

Keywords: Nonlinear-Analysis, Neurocognitive Experiment, Bayesian Model, Cognitive Functions, GoNOGO, ADHD
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1 Introduction

In the last decades, the application of nonlinear analysis and computational modeling in the field of neuroscience has been expanded to some extent that a subfield has emerged as computational neuroscience [13, 16]. The goal of the

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new subfield is to describe how the nervous system processes information in computational and mathematical terms [2, 11, 12]. Understanding the functions of the brain as part of the central nervous system (CNS) has the greatest attention in the field of computational neuroscience [10]. In particular, superior brain functions, which are called Cognitive Functions and enable us to control information, received from external stimuli. Indeed, cognitive functions are the ultimate brain functions that we use to control our behavior in different conditions more effectively [15].

A specific cognitive function is assessed through the experiments representing conditions that the cognitive function is required to make decisions correctly. Hence, to describe cognitive functions through mathematical terms, one should use nonlinear methods to model how individuals make decisions in the condition of real standard-related experiments [18, 19]. The mathematical descriptions should explain the underlying neural mechanisms implemented in the brain, while individuals make decisions in the given condition of experiments [4, 7]. Thus, the current experiments used for modeling at the neuronal implementation level, are the same typical experiments used in behavioral studies. However, it is not clear that the applied experiment conditions are appropriate to represent the neuronal implementation of a cognitive function. Although underlying neural mechanisms of brain functions are analyzed or modeled via different nonlinear methods; the validity of experiments on which the models are based on, is not assessed.

Recently, [1, 6] have developed a Bayesian model (BM) to describe perceptual decision-making (pDM) in the condition of a two-choice pDM task. Using BM, they illustrated that the applied pDM task is not appropriate for investigating the neural implementation of pDM in the brain. BM represents, via a Bayesian inference, how subjects accumulate evidence from the presented stimulus to infer which decision alternative is the correct response. BM is an algorithmic model which computes a posterior belief as a Bayesian inference. However, it can compute other decision variables like log posterior too. Further to the BM, a few other algorithmic models, computing log posterior odds variable, are developed to describe the pDM process [14]. Although all three variables are different representations of the same pDM process; it should be demonstrated which variable is used by the brain [1]. Indeed, it is not clear whether the brain computes posterior belief directly by multiplying all accumulated evidence; or sums the related evidence via computing log posterior odds; or uses log posterior as an inhibited summation. The variables are different in their neural implementations. Hence, by simulating the trajectory of evidence accumulation using the Bayesian model, [1] investigated that measuring neural correlates of DM, in the real conditions of the applied experiment, could not differentiate the variables. Their result demonstrates an important new application of nonlinear methods to validate current behavioral experiments or design new model-based experiments for use in neural measurements.

The experiment condition in the study [1] was simple; so that it does not represent the factors which could affect the individual decision such as task instruction difficulty and reward. Subsequently, in the current study, using BM, we modeled a behavioral dataset related to the GoNoGo task, collected from two groups of children and adolescents with/without ADHD (attention deficit hyperactivity disorder). The GoNoGo task is used to assess Inhibitory Control (IC), which is the most common task used for measuring neural correlates of IC. IC is a cognitive function impaired in individuals with ADHD. Conditions of the task are rewarded and the task instruction is more difficult rather to pDM task. The main aim was first to validate BM by replicating it in a different experiment condition. Secondly, we evaluated the validity of the GoNoGO task for measuring neural correlates of IC, using BM.

2 Task and Behavioral Data

A GoNoGo task [5] was performed to assess IC in two groups of children and adolescents with/without ADHD ages 8-18. The number of subjects in the group of ADHD was 54 (i.e. 15 girls and 39 boys) and the mean age was 8.37 years old. Also, the number of healthy subjects was 83 (i.e. 46 girls and 39 boys) and the mean age was 9.83 years old. The task consisted of 100 independent trials. In each trial, participants saw a horizontal one/two-sided arrow vector in center of a white screen for 100ms (Figure 1). They had to press the arrow key in the same direction as the observed stimulus whether the stimulus was one-sided (Go-trials); and press the no key where the presented stimulus was two-sided (NoGo-trials). 80% of the trials were Go-trial. Inter Stimuli Interval (ISI) presentation was equal to 1500ms. The participants were told to answer as accurately and fast as possible. Furthermore, they got a positive point with each correct answer and also got a negative point for each incorrect answer. The subjects were told that the total number of correct answers¿ 95 is rewarded. We recorded the answer (left/ right, time out and no press) and reaction time (RT) for each trial.

3 Bayesian Model

The Bayesian model, developed by [1], is a reformulation of the Drift Diffusion Model (DDM) of two choice decision tasks [14]. Hence, it represents the basic mechanism of evidence accumulation in the brain, required to infer the correct

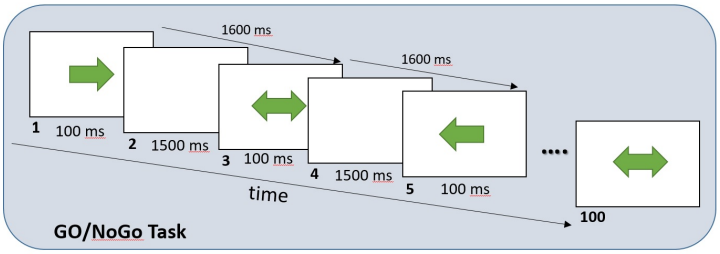

Figure 1: Details of Go/NoGo trials in GoNoGo task

response. In DDM it is assumed that, observing a stimulus, the brain extracts pieces of evidence per time unit, which could be disturbed by noise. Then:

$$y_t - y_{t-\triangle t} = V\triangle t + \sqrt{\triangle t}S\epsilon_t \qquad where\ \epsilon_t \sim N(0,1) \tag{3.1}$$

y_t represent a diffusion state at time t, V is drift rate and S is diffusion rate. Furthermore, we considered ϵ_t as normally distributed noise. $\triangle t$ is also the length of time unit. The evidence units are accumulated over time till the amount reaches sufficient certainty (one of the bounds $\pm B$) to infer the correct action selection. DDM considers each evidence unit as drift and represents the noise, as diffusion. The model also considers the parameter z to account for the preference of participants toward one of the decisions. Thus, z shifts the starting point toward one of the two boundaries. The limitation of DDM is that the model could not explain how evidence units are computed from the sensory input. Therefore, the BM has been developed to explain how the evidence units are generated by observing the stimulus.

BM is a generative model which has 4 principal components, consisting of (1) a generative model of the sensory input process, (2) internal generative model(s) of decision alternatives (3) Bayesian inference as evidence accumulation and (4) a decision threshold to stop accumulation and select an action. BM compares observed stimulus features translated via the sensory input process with the predicted features via the internal generative model and through Bayesian inference, computes the probability of each action given the observed features of stimulus. If the posterior probability of an action touches a predefined threshold, the action will be selected.

3.1 Input process

Brain translates the observed stimuli features to the variable x_t Thus, in each time unit, x_t is generated from a normal distribution (Nd). The mean of Nd is a value corresponded to the noiseless feature of stimulus belongs to Alternative i.

$$x_t \sim N(\mu_i, \triangle t\sigma^2) \tag{3.2}$$

3.2 Internal Generative Model

The task has been explain for the subjects, before performance. Thus, they represent the task alternatives (Press Right, Press Left, No press) in their mind. Thus, BM considers a generative model as Nd for each alternative. The mean of Nd for alternative A_i is a value corresponded to the translated feature of stimulus belongs to A_i. By observing x_t subjects can predict how probability is to generate x_t given the each alternative A_i . Then:

$$P(x_t|A_i) = N(\acute{\mu}_i, \triangle t\acute{\sigma}^{\ 2}). \tag{3.3}$$

If subjects completely learn the instruction we can consider $\mu_i = \acute{\mu}_i$

3.3 Bayesian inference

$$p(A_i|x_t) = \frac{p(x_t|A_1)p(A_1)}{\sum_0^m p(x_t|A_1)p(A_1)} \tag{3.4}$$

$$p(A_i|X_{1:t}) = \frac{p(x_t|A_i)p(A_i|X_{1:t-1})}{\sum_0^m p(x_t|A_j)(A_i|X_{1:t-1})} \tag{3.5}$$

$$X_{1:t} = x_1, ..., x_t$$

Table 1: Mean of prior and posterior distributions of extended Baysian Model parameters for GoNoGo task in ADHD and Control groups

Estimated Parameters		Prior mean (std)	ADHD	Control
name	*Distribution*		*Posterior mean (std)*	
λ	Uniform	0 (1)	0.93 (0.01)	0.74 (0.01)
σ	log-normal	0.01 (1)	275.11 (15.23)	205.837 (34.65)
η	log-normal	0.1 (1)	0.0005 (0.0003)	0.0003 (0.0001)
P_0	Uniform	0 (1)	0.57 (0.01)	0.48 (0.01)
std_{p_0}	log-normal	0.05 (1)	0.02 (0.01)	0.04 (0.01)
T_{nd}	log-normal	0.5 (1)	0.055 (0.02)	0.51 (0.01)
$Std_{T_{nd}}$	log-normal	0.15 (1.3)	0.1 (0.002)	0.58 (0.005)

3.4 Decision Policy

Decision is made for the alternative with the largest $p(A_i|x_t)$:

$$\max_i \; p(A_i|X_{1:t}) \geq \lambda \tag{3.6}$$

$$\max_i \; p(A_i|X_{1:t}) \geq \acute{\lambda} \tag{3.7}$$

$$\left|\log \frac{p(A_1|X_{1:t})}{p(A_2|X_{1:t})}\right| \geq \lambda^*. \tag{3.8}$$

In addition, the BM consider the parameter T_{nd} which represent delay, may resulted from basic sensory processing and motor production as a non-decision time.

3.5 Parameter Estimation

We simulated the extended version of BM (eBM) which insert inter-trial variability in the BM model [6] by modeling the parameters as distributions. So that, noise level (σ) of input process in different trials generated from ln $N(\mu_0, \eta)$. in addition non-decision time (T_{nd}) and subjects bias p0 are generated from ln $N(\mu_{T_{nd}}, S_t)$ and Uniform $(p_0 - S_{p_0}/2, p_0 = S_{p_0}/2)$ respectively. All the scripts developed in Python 3.7.

We estimated the parameters for each model from the recorded behavioral data, using a second level Bayesian inference method so-called Expectation Propagation-Approximation Bayesian Computation (EP-ABC) [3]. We ran EP-ABC algorithm for each participant in each group separately. EP-ABC returns posterior parameters distribution of participants. The parameter means over all participants of each groups and the related standard deviation for each model are listed in Table 1.

4 Simulating evidence accumulation trajectories

After data fitting and parameter estimations, we simulated evidence accumulation trajectories for three computed variables (3.6), (3.7) and (3.8) including posterior belief, log posterior and log posterior odds. We set model parameters to the posterior means inferred from behavioral data collected in the real conditions of the GoNoGo task (Table 2). We consider that by reaching a sufficient number of evidence, the asymptotic behavior of the model variables could represent their potential differences. Hence, we simulated the trajectory of evidence accumulation of each variable in two conditions (applying a bound and without applying a bound). Simulating without applying a bound (λ : uncertainty threshold) could represent the conditions with a sufficient number of evidence. However, as subjects should respond to task stimuli as fast as possible, we have to apply a bound to simulate the real condition of the experiment. λ represents that evidence accumulation is stopped when a subject makes a decision. We assess whether the trajectories in the experiment conditions are the same as conditions with high certainty.

Table 2: Results of t-test for eBM parameters comparing in ADHD and Control groups

Parameters	ADHD	Control	P-value
σ	275.11 (15.23)	205.837 (34.65)	0.0001
$\acute{\sigma}$	9.34 (0.175)	10.84 (0.098)	0.0001
T_{nd}	0.55 (0.02)	0.51 (0.01)	0.001

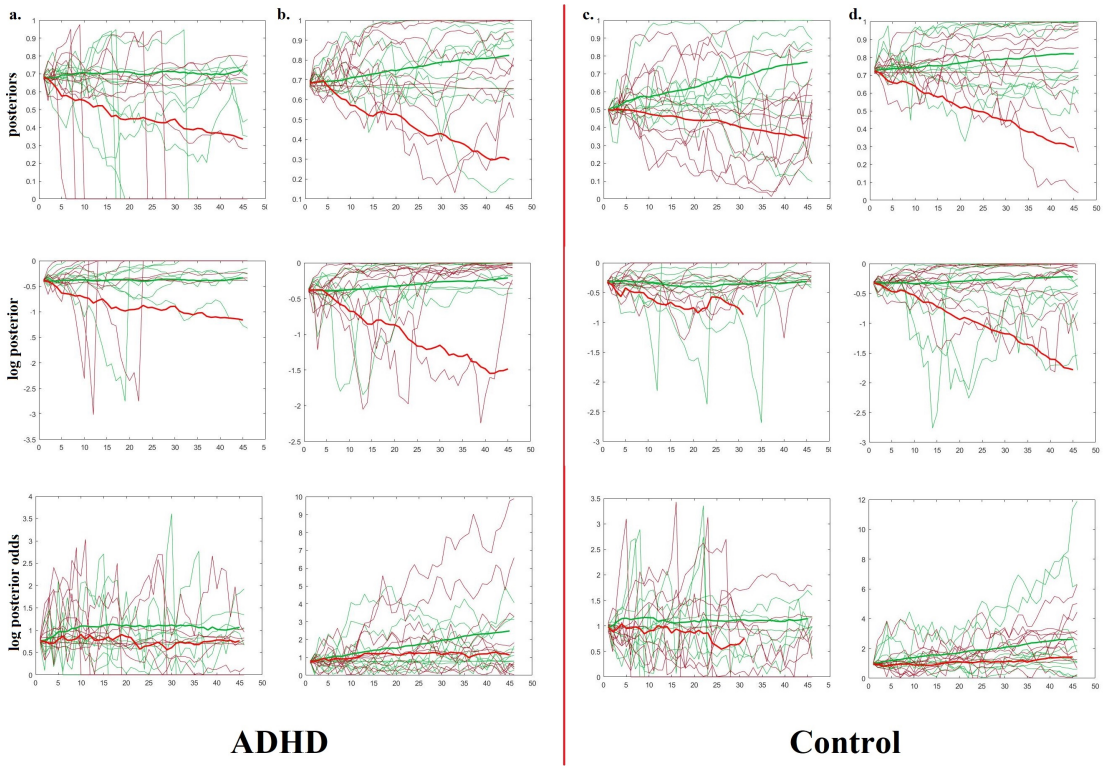

Figure 2: Trajectories of eBM model variables including posterior, log posterior and log posterior odds, separated with groups. (a. and c.) are in condition of rewarded go-trial of GoNoGo task and (b. and d.) are in condition without applying the bound λ)

5 Results

We estimated eBM parameters for each individual in each group separately. Then, we simulated the data point of the answer (left or right) and the RT for each group and did a simple paired t-test between the behavioral and stimulated data for each group. The results demonstrated that matches were significant for both groups as the p-values of paired t-test were higher than 0.05 ($p-value_{ADHD} = 0.453, p-valuse_{Control} = 0.234$). Furthermore, we compared the stimulus noise-level (σ) subject uncertainty (σ) and no-decision time (T_{nd}) in ADHD and control groups. We used a t-test for each parameter. The results were significant for all three parameters. The results were significant for all three parameters ($p - value < 0.001$) the details mentioned in Table 2.

Furthermore, we simulated the trajectories of three model variables for exactly the same input, in the condition of Go-trial in the GoNoGo task. The result illustrated that the model may not be differentiated through the GoNoGo real condition. Figure 2 illustrates variable trajectories for ADHD and control groups separately. Although the patterns of evidence accumulation in the condition of the experiment (shape of trajectories) are similar to the corresponding condition without applying (λ); they would not closely resemble the asymptotic behaviors in these conditions.

6 Conclusion

As a case- study of a Bayesian model, we demonstrated the essential for model-based validation of cognitive experiments before being applied to model neuronal implementations of cognitive functions. Using eBM, we describe

how individuals make decisions in the condition of the GoNoGo task that IC is required to choose decision alternatives correctly. In addition, by comparing eBM parameters in groups of children/adolescents with and without ADHD, we investigate which model parameter could represent group differences. Furthermore, we simulated the trajectory of three model variables, describing the decision process in the brain, to differentiate their asymptotic behaviors, when reaching a sufficient number of evidence for making a decision. However, their behavior could not closely resemble the asymptotic behavior in high certainty conditions. It means that by measuring neural correlates of IC while performing the GoNoGo task, we may not investigate how subjects accumulate evidence in the brain to decide on the correct response to the presented stimulus. Therefore, although differences in performing GoNoGO tasks could distinguish individuals based on their IC skills; it may not give more robust information on neural correlates of IC in the brain. The finding could account for inconsistent or conflicting results of neuroimaging studies using the GoNoGo task which compared ADHD and control groups [8, 9]. So the results of recent neuro-imaging meta-analysis on functional MRI (fMRI) studies, using IC tasks on children and adolescents with and without ADHD are not convergent [17].

As [1] mentioned in their study, rewarded (increased λ) conditions may differentiate the DM variables, However, our finding investigated that in the rewarded condition of the GoNoGo task, we may not investigate which variable is used by the brain. It means that changing the values of model parameters may not help to experimentally investigate how the brain accumulates DM alternative evidence. Therefore, new computational models are needed to extend the model or reformulate it; so that their new parameters could characterise more details of evidence accumulation. For example, eBM accounts for accumulation variability based on noise level and internal uncertainty of individuals. However, it is not clear which sources lead to these variabilities, represented as uncertainty and noise level.

We can conclude that typical experiments used for assessing cognitive functions behaviourally, may are not valid to represent related underlying mechanisms in the brain. On the other hand, computational descriptions of underlying mechanisms of cognitive functions should be validated by fitting to the behavioural data. Hence, they had to represent individual performance in the condition of experiments. It means that we could not first measure neural correlates and model neural implementations of cognitive functions and design the behavioural experiments based on the results. Thus, the next important step of applying non-linear methods in neuroscience is to validate the typical experiments through algorithmic models of related cognitive functions. In addition, they should be used to extend the current models and cover their restrictions so that new appropriate experiment conditions, for the neuronal implementation level, could be simulated by the models.

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