Modelling reaction time distribution in schizophrenia with Ratcliff's Diffusion Model

N. Andreakos[a], N. Smyrnis[a,b]

a. Laboratory of Sensorimotor Control, University Mental Health Research Institute, Athens, Greece.

b. Psychiatry Department, National and Kapodistrian University of Athens, Medical School, Athens, Greece.

Abstract

Slowing of processing speed is observed in patients with schizophrenia. In this study 26 patients with schizophrenia, 15 siblings of patients and 25 healthy controls performed an oddball task of varying working memory load. Use of the Drift Diffusion Model (DDM) showed a decrease in the speed of the basic decision process (diffusion drift rate (*v*)) in patients and relatives compared to controls. Also an increase in the mean of the non-decisional processing time (*t0*) was present only for patients. These results could provide evidence for the heritability of the decrease in the speed of decision processing in schizophrenia that could be shared with other mental disorders such as Attention Deficit Hyperactivity Disorder.

Introduction

Schizophrenia is a mental disorder that usually appears in late adolescence or early adulthood. Characterized by abnormal social behavior and common symptoms include false beliefs, unclear or confused thinking, hearing voices that others do not, reduced social engagement and emotional expression, and a lack of motivation (National Institute of Mental Health). People with schizophrenia often have additional mental health problems such as anxiety, depressive, or substance-use disorders (Buckley et all., 2009). Symptoms typically occur gradually, begin in young adulthood and last a long time.

Patients with schizophrenia are slower than healthy controls in a large variety of fast decision tasks in which reaction time (RT) is measured (Nuechterlein, 1977; Cadenhead et al., 1997). Intra-Subject Variability (ISV) measures the variance of the RT distribution and some studies propose that this measure indicates cognitive and sensorimotor processing stability and is not simply a by-product of increased mean RT (Rentrop et al., 2010; Kuntsi & Klein, 2011).

RT-ISV has been confirmed as a reliable measure dissociating individuals with ADHD from healthy controls. (Klein et al. 2006; Kuntsi and Klein 2011; Kofler et al. 2014). Similar differences have been found in patients with schizophrenia. Schwartz et al. (1989) used a simple manual response task to find, if there are differences between mean RT and RT-ISV in groups with psychotic symptoms (schizophrenia and affective disorders). Mean RT is a specific predictor of the inability of the patients to maintain a cognitive set, whereas RT-ISV is a specific predictor of the severity of psychotic and disorganisation symptoms (Vinogradov et al., 1998). It was found, that mean RT was larger for all groups, whereas RT-ISV was larger specifically for schizophrenia patients. Kaiser et al. (2008) compared RT-ISV of schizophrenia, major depression and borderline personality disorder patients and found that the RT-ISV clearly dissociated schizophrenia patients from all other groups. In a visually guided saccade task increased RT-ISV but not mean RT was observed in patients with schizophrenia compared to healthy controls (Smyrnis et al. 2009).

A theoretical model of the underlying cognitive processes that was developed to explain the behaviour both in terms of accuracy and RT distribution characteristics in

fast two-choice RT tasks was the Drift Diffusion Model (DDM; Ratcliff 1978; 1979; Ratcliff and McKoon, 2008). «According to this model, a choice should be made, when the evidence of the winning alternative are more than the evidence of the losing alternative and the difference between them exceeds a threshold» (Bogacz, 2007). Bogacz used these terms to delineate the choice, which was made by the individual (winning alternative) and the choice, which wasn't selected (losing alternative). The DDM includes one integrator -instead of two, which are used by other models, such as Race Model- that accumulates the difference between the evidence for the two alternatives. When the level of the integrator's activity reaches a positive or a negative threshold, then the decision is made (Bogacz, 2007).

The diffusion model assumes that decisions are made by a noisy process that accumulates information over time from a starting point toward one of two response criteria or boundaries (Ratcliff and McKoon, 2008). There is noise (within-trial variability) in the accumulation of information so that processes with the same mean drift rate (*v*) do not always terminate at the same time (producing RT distributions) and do not always terminate at the same boundary (producing errors) (Ratcliff and McKoon, 2008). The DDM model also assumes that the total RT is the sum of the non-decisional processes -stimulus encoding-, the response execution and the decisional process, which is mentioned above. The parameters of the DDM that correspond to the non-decisional processes are the mean RT for these processes (*t0*) and its standard deviation (SD) across trials (*st0*). The decision related parameters of the DDM are the starting point of the decision process (*zr*), the boundary where the decision process ends *(a-0)* and the mean diffusion rate (*v*), in which the individual begins to collect the appropriate amount of information, which is needed to respond. There are two boundaries for the alternative responses and their separation represents the average amount of required information in order for the participant to reach a decision. If the start point (*zr*) lies in the middle of the two boundaries, then there is no bias favoring one of the responses.

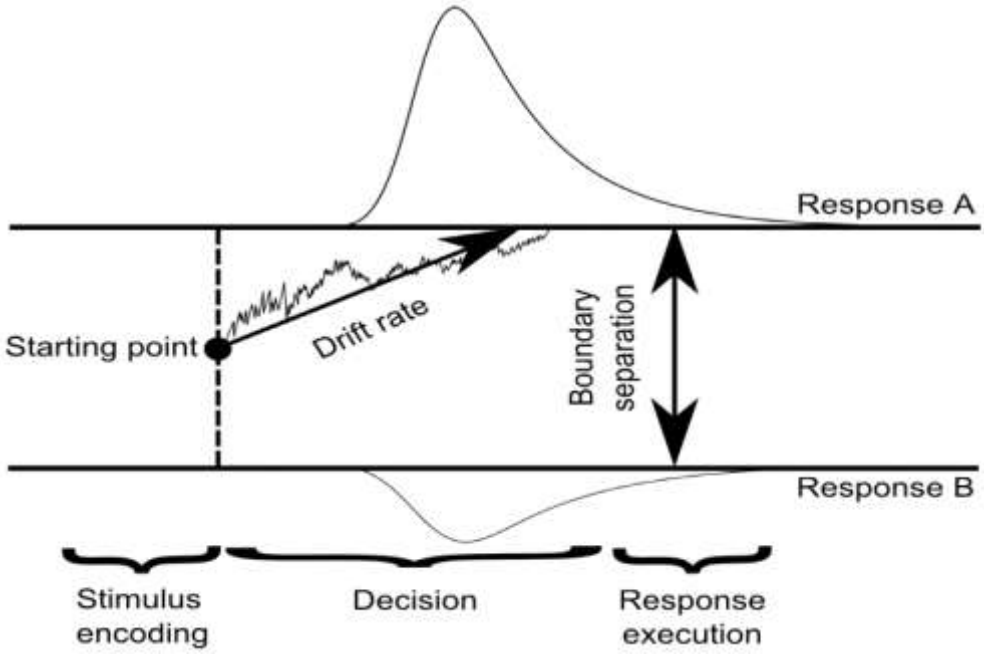

Figure 1. These are the parameters of DDM. The individual is between two responses (A or B). Boundary separation *(a-0)*, starting point *(zr)*, drift rate *(v)* and stimulus encoding – response execution *(t0)*.

Many studies in the past decade used DDM to model cognitive processes in two choice RT tasks in clinical populations (Ratcliff et al 2016). A few studies have investigated the parameters of the DDM model in ADHD. Mulder et al. (2010) found that there was no difference in ADHD patients and controls for mean diffusion rate and non-decisional time (*t0*) but only a smaller separation threshold (*a*) in the condition where accuracy was required. Also, a significant decrease in non-decisional time (*t0*) for ADHD patients compared to controls was observed in some of these studies (Karalunas and Huang-Pollock 2013; Metin et al., 2013). Only one study far applied the DDM in schizophrenia patients. Moustafa et al. (2015) applied the DDM to a reward and punishment learning task and reported increased non-decisional processing time (*t0*), higher separation threshold (*a*) as well as a lower drift diffusion rate *(v)* specifically for punishment trials in patients compared to controls.

The present study aimed to model RT distribution in a simple decision task in schizophrenia patients and their first degree relatives in order to identify, which of the modelled processes that are deviant in these patients have state dependent and which

trait dependent characteristics. Schizophrenia patients, siblings of patients and healthy controls performed a combined two-choice oddball, verbal n-back task. Performance accuracy as well as RT distribution parameters was measured for each individual. The RT distributions were then modelled using the DDM model. RT model parameters were compared among patients, siblings and healthy controls.

Methods

1. Sample

The study sample consisted of 26 patients with schizophrenia (22 men and 4 women), 15 healthy siblings of other untested patients with schizophrenia (4 men and 11 women) and 25 healthy controls (15 men and 10 women). A one-way analysis of variance (ANOVA) showed no age difference among groups (patients: Mean=37 years, SD=10; relatives: Mean=37 years SD=14; controls: Mean=31years SD=9; F (2, 63) =3.17, p=.245). All patients were recruited from the Centre for Rehabilitation of the Psychiatry Department of the National and Kapodistrian University of Athens.

First-degree relatives and healthy controls were excluded if they were currently taking rescribed medication or if they stated personal history of psychiatric or neurological disorder. All participants agreed to participate voluntarily in the study and signed a written informed consent. The study protocol was approved by the ethics committee of the Eginition University Hospital.

2. Procedure

The experiment comprised of two tasks: the 0-back and the 1-back task and two stimulus conditions within each task (oddball: 25% frequency and standard: 75% frequency). In the 0-back task the oddball stimulus was the letter ‘O’ and for the 1-back, every trial that was identical to the preceding one. Each participant completed 3 blocks of each task in the sequence A, B, A, B, A, B. Both tasks consisted of 160 trials per block, of which 40 were oddballs and 120 were standards. The order that participants completed the tasks was counterbalanced.

Data Analysis

We used the "fast-dm-30" program (http://www.psychologie.uni-heidelberg.de/ae/meth/fast-dm/; Voss and Voss 2007; 2008) to compute the parameters of the DDM of Ratcliff (1978) for each subject. The model was used separately for each block of trials for each task (0-back, 1-back) for each subject. The two stimulus conditions (odd and standard) were used to derive separate diffusion

rates *v*. Thus according to the DDM, *zr*, *a*, *v (odd)*, *v (standard)*, *t0* and *st0* were calculated for each block and each task. The values for separate blocks of each task were then averaged for each subject. The goodness of fit of a statistical model describes how well it fits a set of observations. Measures of goodness of fit typically summarize the discrepancy between observed values and the values expected under the model in question. Such measures can be used in statistical hypothesis testing (Qiang et all., 2016). The Kolmogorov–Smirnov test (K–S test or KS test) is a nonparametric test of the equality of continuous, one-dimensional probability distributions that can be used to compare a sample with a reference probability distribution (one-sample K–S test), or to compare two samples (two-sample K–S test). In this study, we used Kolmogorov-Smirnov (K -S) test method because the number of trials per task were higher than 100 and lower than 500, which is the span of using this criterion. The estimation procedure was fit for all runs of DDM (*p*-values of the K-S test were all above 0.05).

A 3x2 mixed model MANOVA was applied or the DDM parameters *zr, a, v_1, t0, st0 and v_0*. Group and task was the independent variable. Planned comparisons among different group means were performed to test, whether there were differences between groups.

All statistical analyses were performed using the IBM SPSS Statistics (v23).

Results

zr

The mean *zr* values for each task are presented in Table 1. There was a significant effect of task on the starting point bias ($F_{1,63}$ = 27435, $p < 10^{-6}$, η^2 = .18). There was no effect on group on the diffusion process starting point bias *zr* ($F_{2,63}$ = .529, p = .59). There was no significant group by task interaction ($F_{2,63}$ = .389, p = .678).

a

The threshold separation value *a* was not different between the two tasks as shown in Table 1 ($F_{1,63}$ = .034, p =.86). The threshold separation *a* was significantly different among groups ($F_{2,63}$ = 3.5, p = .032) although planned comparisons did not reveal significant differences (patients vs controls (p = .104), patients vs realtives (p = .683) and controls vs relatives (p = .318).

v

Table 1 presents the diffusion rate *v* for different stimulus conditions and tasks. The diffusion rate *v* was significantly larger for standard compared to oddball trials ($F_{1,63}$ = 116.4, $p < 10^{-6}$, η^2 = .47) and for 0-back compared to 1-back tasks ($F_{1,63}$ = 51.7, $p < 10^{-6}$, η^2 = .29). There was a significant effect of group on the diffusion rate *v* ($F_{2,63}$ = 8.6, $p <10^{-3}$, η^2 = .12). Planned comparisons revealed that the diffusion rate *v* was significantly larger for controls than patients ($p < 10^{-3}$) while the difference between relatives and controls and relatives and patients did not reach significance (p = .14 and p = .37 respectively). There was no significant group by task interaction ($F_{1,63}$ = .3, p = .76) nor three way interaction ($F_{2,63}$ = .83, p = .44).

t0

The mean RT for non-decisional processes, *t0*, was significantly larger for the 1-back compared to the 0-back task ($F_{1,63}$ = 36.4, $p < 10^{-5}$, η^2 = .22). There was also a significant effect of group on *t0* ($F_{2,63}$ = 17.01, $p < 10^{-3}$, η^2 = .21). Patients had significantly larger *t0* compared to controls (p = 0.004) while the difference between relatives and patients and relatives and controls were not significant (p = .87 and p =

.30 respectively). There was no significant interaction of group and task ($F_{2,63}$ = 1.2, p = .31).

st0

There was a significant effect of task on the variability of the non-decisional RT *st0* ($F_{1,63}$ = 7.2, p =.008, η^2 = .05) with larger variability for the 1-back compared to the 0-back task (Table 1). There was also a significant effect of group on *st0* ($F_{2,63}$ = 15.8, $p < 10^{-3}$.12, η^2 = .20). Patients had significantly larger RT variability than controls ($p < 10^{-3}$) and relatives ($p = .021$) while relatives did not differ from patients (p = .34).

	Task		**Group**		
	0-back	**1-back**	**Patients**	**Relatives**	**Controls**
zr	.55 (.01)	.47(.01)	.50 (.01)	.52(.01)	.51(.01)
a	1.23(.03)	1.24(.03)	1.26 (.04)	1.29(.04)	1.15(.04)
v	4.9 (.15)	3.7(.15)	3.9(.16)	4.4 (.21)	4.8 (.16)
t0	278 (5)	319(5)	318 (7)	304 (7)	274(5)
st0	113 (7)	141(7)	161 (11)	125(8)	95(8)

Table 1: Means for each stimulus condition, task and group for all DDM parameters.

Note: The diffusion model parameters *zr* (starting point), *a* (boundary separation) and *v* (mean diffusion rate) are expressed in arbitrary units while *t0* (mean non-decisional

RT) and *st0* (SD of the non-decisional RT) are expressed in msec. Standard error of each mean in parentheses.

Discussion

In some studies, slowing of processing speed is observed in patients with schizophrenia (see introduction). In this study, we wanted to identify, if there are any differences in DDM modelled processes between patients, relatives and controls, which can let us confirm these evidences or discover any others. Use of the Drift Diffusion Model (DDM) showed a decrease in the speed of the basic decision process (diffusion drift rate (*v*)) in patients and relatives compared to controls and an increase in the mean of the non-decisional processing time (*t0*), which was present only for patients. These results could provide evidence for the heritability of the decrease in the speed of decision processing in schizophrenia.

We decided to use the DDM, because it allowed us to decompose the RT into different cognitive parameters and study the differences among our groups. In the only other study, in which DDM was used to analyse behavior in a probabilistic classification learning task in schizophrenia, Moustafa et al. (2015) found that patients had a significant decrease in mean diffusion rate (*v*) that was observed specifically in trials that were followed by punishment. We observed a decrease in the mean diffusion rate for patients, which was independent of task and stimulus condition. This evident lead us to suggest that maybe there is a general deficit in the decision process in these patients. We also showed that patients and siblings were dissociated from healthy controls by the differences in the rate of the decision process (the rate v for relatives was in between patients and controls) and maybe there is a trait and not state dependent characteristic of the disorder.

In decision threshold (*a*) for patients, we observed an increase compare to controls, which didn't prevail planned comparison testing Also there were no differences between relatives and patients or controls and was independent of task. An increase in decision threshold was also observed in the study of Moustafa et al. (2015). We also observed that the decision threshold was overall significantly higher in women than men independent of status (patients, relatives or controls) and that could indicate that the response style may be influenced by individual factors such as gender. Future studies are needed to confirm this hypothesis.

An increase of the mean non-decision time (*t0*) in patients, which was also observed in the previous study of Moustafa et al. (2015), dissociated patients from healthy controls. Antipsychotic medication acting on the motor system might affect

non-decisional sensorimotor time and one could hypothesize that this increase in the non-decisional component of the RT might not be present in first episode drug naive patients. This hypothesis could be tested in future studies.

Finally, the increase in the variance of the non-decisional component of RT *(st0)* showed a state dependency being increased in patients compare to controls and relatives. In the previous study of DDM (Moustafa et al., 2015) in schizophrenia this parameter was not included in the model. This parameter showed us that patients differ significantly from controls and relatives and that may reveal problems in cognitive and sensorimotor processing stability.

As mentioned in the introduction a number of studies used the DDM model to study cognitive processes underlying RT in fast decision tasks in children with ADHD. The DDM model was also used to study cognitive processes underlying RT in fast decision tasks in children with ADHD. Most of the studies showed that the diffusion rate (*v*) decreased in patients with ADHD and a few studies showed a decrease in boundary separation (*a*). Finally the non-decisional time (*t0*) was found to be decreased in patients with ADHD compared to controls in some studies (see introduction). Thus the DDM analysis provides further insight into the similarities and differences in fast decision processing between ADHD and schizophrenia.

A general decrease in the mean rate of the decision process *(v)* seems to be common in both disorders. Moreover this decrease in the rate of the decision process has trait characteristics in schizophrenia. So far the DDM model has not been performed in relatives of patients with ADHD. If a similar trait dependency of the decrease in the rate of the decision process is confirmed for ADHD this could provide the ground for the study of shared heritability of basic cognitive processes in these two disorders and its neurobiological substrate, suggesting the presence of a heritable trait in cognition that is shared in schizophrenia and ADHD. Recent studies have suggested shared genetic background for these two disorders (Keshavan et al., 2011; Larsson et al., 2013).

But there is also some differences between these two diseases. The threshold *(a)* decreases in ADHD is slightly increased in schizophrenia (Huang-Pollock et al., 2012; Huang-Pollock et al., 2016; Weigard and Huang-Pollock, 2014). The reason is that ADHD has been linked to an increased impulsivity in behaviour and schizophrenia has been linked to a general decrease in impulsivity and overall

decrease in goal directed behavior as a result of negative symptoms (Egeland, 2007). Also the non-decisional processing time *(t0)* differs between the two disorders (see introduction). Feature time is increased in schizophrenia patients and is decreased in patients with ADHD compared to healthy controls. In any case one could speculate that different mechanisms related to sensory and motor processing might affect this component of the RT distribution in each disorder.

In conclusion this study confirmed that patients have a deficit in the speed of processing in a simple decision task in schizophrenia that has trait and state characteristics. Modelling the cognitive processes underlying the RT distribution using the DDM model, revealed a specific deficit in the rate of the decision processes, with trait characteristics and an increase in the variance of the non-decisional sensorimotor processing time that had state characteristics. The deficit in the rate of the decision process is shared with ADHD patients. Future research could provide further evidence for the existence of a shared familial trait in the speed of cognitive processing between schizophrenia and ADHD.

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References

Bogacz, R., 2007. Optimal decision-making theories: linking neurobiology with behaviour. Trends in Cognitive Science, 188-125.

Buckley, P.F., Miller, B.J., Lehrer, D.S., Castle, D.J., 2009. Psychiatric comorbidities and schizophrenia. Schizophrenia Bulletin. 35, 383–402.

Cadenhead, K.S., Geyer, M.A., Butler, R.W., Perry, W., Sprock, J., Braff, D.L., 1997. Information processing deficits of schizophrenia patients: relationship to clinical ratings, gender and medication status. Schizophrenia Research 28, 51-62.

Egeland, Jens. 2007. Differentiating attention deficit in adult ADHD and schizophrenia. Archives of Clinical Neuropsychology. Elsevier, 763-771.

Huang-Pollock, C.L., Karalunas, S.L., Tam, H., & Moore, A.N., 2012. Evaluating vigilance deficits in ADHD: a meta-analysis of CPT performance. Journal of Abnormal Psychology 121 (2), 360-371.

Huang-Pollock, C.L., Ratcliff, R., McKoon, G., Shapiro, Z., Weigard, A., Galloway-Long, H. 2017. Using the Diffusion Model to Explain Cognitive Deficits in Attention Deficit Hyperactivity Disorder. Springer Science + Business Media New York 2016.

Kaiser, S., Roth, A., Rentrop, M., Friederich, H.C., Bender, S., Weisbrod, M., 2008. Intra-individual reaction time variability in schizophrenia, depression and borderline personality disorder. Brain and Cognition 66, 73–82.

Karalunas, S.L., & Huang-Pollock, C.L., 2013. Integrating impairments in reaction time and executive function using a diffusion model framework. Journal of abnormal child psychology 41 (5), 837-850.

Keshavan. M., Montrose, Rajarethinam, R., Diwadkar, V., Prasad, K., Sweeney, J.A., 2011. Psychopathology among offspring of parents with schizophrenia: Relationship to premormid impairments. Schizophrenia Research 103(1-3), 114-120.

Klein, C., Wendling, K., Huettner, P., Ruder, H., Peper, M., 2006. Intra-subject variability in attention-deficit hyperactivity disorder. Biological Psychiatry 60, 1088–1097.

Kofler, M.J., Alderson, R.M., Raiker, J.S., Bolden, J., Sarver, D.E., & Rapport, M.D., 2014. Working memory and intraindividual variability as neurocognitive indicators in ADHD: examining competing model predictions. Neuropsychology 28 (3), 459.

Kuntsi, J., Klein, C., 2011. Intra-individual variability in ADHD and its implications for research of causal links. In Stanford, C., Tannock, R. (Eds.), Behavioral Neurobiology of ADHD and its Treatment. Current Topics in Behavioral Neuroscience 9, 67–92.

Liu, Qiang, Lee, Jason, Jordan, Michael. 2016. A Kernelized Stein Discrepancy for Goodness-of-fit Tests. The 33rd International Conference on Machine Learning. New York, USA: Proceedings of Machine Learning Research, 276–284.

Metin, B., Roeyers, H., Wiersema, J. R., van der Meere, J. J., Thompson, M., & Sonuga-Barke, E., 2013. ADHD performance reflects inefficient but not impulsive information processing: A diffusion model analysis. Neuropsychology 27 (2), 193.

Moustafa, A.A., Kéri, S., Somlai, Z., Balsdon, T., Frydecka, D., Misiak, B., & White, C., 2015. Drift diffusion model of reward and punishment learning in schizophrenia: modelling and experimental data. Behavioural brain research 291, 147-154.

Mulder M.J., Bos D., Weusten J.M.H., van Belle J., van Dijk S.C., Simen P.,

van Engeland H., & Durston S., 2010. Basic Impairments in Regulating the Speed-Accuracy Tradeoff Predict Symptoms of Attention-Deficit/Hyperactivity Disorder. Biological Psychiatry 68, 1114–1119.

National Institute of Mental Health. January 2016. Schizophrenia. Archived from the original on 25 November 2016. Retrieved 3 February 2016.

Nuechterlein, K.H., 1977. Reaction time and attention in schizophrenia: a critical evaluation of the data and theories. Schizophrenia Bulletin 3, 373–428.

Ratcliff, R., 1978. A theory of memory retrieval. Psychological review 85, (2) 59.

Ratcliff, R., 1979. Group reaction time distributions and an analysis of distribution statistics. Psychological Bulletin 86, 446-461.

Ratcliff, R., & McKoon, G., 2008. The diffusion decision model: theory and data for two-choice decision tasks. Neural computation 20 (4), 873-922.

Rentrop, M., Rodewald, K., Roth, A., Simon, J., Walther, S., Fiedler, P., Weisbrod, M.,Kaiser, S., 2010. Intra-individual variability in high-functioning patients with schizophrenia. Psychiatry Research 178 27–32.

Schwartz, F., Carr, A.C., Munich, R.L., Glauber, S., Lesser, B., & Murray, J., 1989. Reaction time impairment in schizophrenia and affective illness: the role of attention. Biological psychiatry 25(5), 540-548.

Smyrnis, N., Karantinos, T., Malogiannis, I., Theleritis, C., Mantas, A., Stefanis, N.C.,Hatzimanolis, J., Evdokimidis, I., 2009. Larger variability of saccadic reaction times in schizophrenia patients. Psychiatry Research 168, 129–136.

Vinogradov, S., Poole, J.H., Willis-Shore, J., Ober, B.A., Shenaut, G.K., 1998. Slower and more variable reaction times in schizophrenia: what do they signify? Schizophrenia Research 32, 183–190.

Voss, A., & Voss, J., 2007. Fast-dm: A free program for efficient diffusion model analysis. Behavior Research Methods 39 (4), 767-775.

Voss, A., & Voss, J., 2008. A fast numerical algorithm for the estimation of diffusion model parameters. Journal of Mathematical Psychology 52 (1), 1-9.

Weigard, A., & Huang-Pollock, C., 2014. A diffusion modelling approach to understanding contextual cueing effects in children with ADHD. Journal of Child Psychology and Psychiatry 55 (12), 1336-1344.