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Variability, Noise and Predictability in Motor Response Times: Adaptation or Misadaptation?

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1. Introduction

The ability to maintain a focus of attention on a selected item is crucial for complex and adapted behaviors. In the wild, a predator must be able to track the appearance of other animals while pursuing a prey when the prey must be able to focus on its surrounding environment in order to avoid unexpected obstacles. To survive both predator and prey must share this ability to dissociate the focus of attention and the orientation of gaze. In the context of a laboratory the study of this ability to sustain attention has often been examined using tasks which require individuals to actively maintain performance speed and accuracy over long testing period (von Voss, 1899; Kraepelin, 1902; Robinson & Bills, 1924; Russo & Vignolo, 1967; Rabbitt, 1969; Rabbitt, 1980; Sanders & Hoogenboom, 1970; Richer and Lepage, 1996). In practice, these tasks require subjects to be engaged in repetitive activities such as simply detecting visual objects presented on computer screens. During these repetitive activities performance of subjects varies and evidence concerning the salience of intra-individual-variability to the study of behavior is becoming a compelling reminder that the prevailing emphasis on one of the seemingly most fundamental concepts in traditional differential psychology represents an oversimplification that can hinder the search for powerful and general lawful relationships (Nesselroade, J.R., et al., 2002).

In the last decades, new methodological approaches have improved research in intra-individual-variability. These methods are accounting for both the deterministic and the stochastic components of psychological processes at the intra-individual level. Finally, tools have been developed to account beyond individual differences in variance and covariance of latent variables given measurement invariance. Today, the concerns are now less about whether variability within an individual should be studied than it is about how to make use of this important source of information to assess psychological processes. Authors such as Sliwinski, Almeida, Smuth, & Stawski (2009); MacDonald, Nyberg, & Bäckman (2009) and many others are writing about how to best use both sources of information together to illustrate, how short term variability over time can differ between people in diagnostically interesting ways. In fact, it may be time to make the case that the amount of variability is less a focus than is the time dynamics of the variability particularly in the studies of ADHD.

Ram and colleagues (2009) make even the case that the time structure of intra-individual-variability needs to be considered along with what they call the net variability. Intra-individual-variability is, in some sense, the intellectual parent of dynamical systems analysis in psychology. Because, ADHD subjects demonstrated significantly more variable performance than controls and because numerous studies supports intra-individual variability as a hallmark feature of ADHD beyond the domain of response inhibition and reinforces, there is a crucial need to fully consider variability in ADHD more broadly.

2. Intra-individual variability

Typically, the global measures of speed and accuracy are used to determine an individual's ability to sustain attention. However an important limit of all measures reflecting central tendency is that they only coarsely summarize the full response time (RT) distribution, without capturing potentially useful information on intra-individual RT variability (Carpenter and William, 1995; Larson & Alderton, 1990; Rabbitt, Osman, Moore, & Stollery, 2001). In fact, RT distributions are often asymmetrical: they have a steep slope on the left side which is due to a rather narrow range of very fast responses, and they have an elongated right tail, arising from a substantial amount of more broadly distributed slow responses (Leth-Steensen, Elbaz, & Douglas, 2000; Logan, 1992). Recent studies have shown that subjects with attention-deficit/hyperactivity disorder present larger response variability across a variety of speeded-reaction time tasks, laboratories, and cultures (see for review, Castellanos and Tannock, 2002). This high response variability is informative because it may reflect intrinsic properties that extend far beyond the distributional properties of RTs (Gilden and Hancock 2007; Pouget et al. 2010; Pouget et al. 2011). Because RTs are almost always collected in large blocks of trials, the natural ordering of trials generates historical record and the RT records have been shown to have characteristic structures (Gilden, 1997, 2001; Thornton & Gilden, 2005; Van Orden, Holden, & Turvey, 2003, 2005; see also Nelson et al. 2010; Emeric et al. 2007). In particular, it is now well established that RT sequences in normal adults often show evidence of a long-term memory process known as $1/f$ noise (Gilden, 2001; Thornton & Gilden, 2005), so named because its power spectrum falls inversely with frequency. This kind of noise is found in that part of the data generally regarded as unexplained variance, the trial-to-trial residual variability. More generally, this power-law scaling relation implies that results of a measurement depend on the measurement scale or sampling unit used to take the measurement (over a finite range of scales). Power-law scaling relations, linear relations between the logarithms of the scale and the logarithms of the measurement result, are commonly observed of natural phenomena described using fractal geometry and are symptomatic of self-similar patterns (Bassingthwaight et al., 1994). In ADHD, the result of a measurement of a natural fractal is also amplified in proportion to the measurement scale Response time variability measures aspects of executive functioning related to a person's ability to consistently focus and purposefully sustain mental effort. With prolonged time on task, work speed has been observed not only to become slower but also less regular (Gilden, 2001; Thornton & Gilden, 2005). For example, von Voss (1899) observed that with prolonged work on a digit addition task, the frequency of long responses increased whereas there was no change in the fastest responses. The question of what causes the characteristic work speed fluctuations is still unresolved (Weissman, Roberts, Visscher, & Woldorff, 2006; but see Gilden, 2001; Thornton

& Gilden, 2005; Pouget et al. 2011). Previous investigations into the nature of intraindividual RT variability drew the conclusion that occasionally occurring attentional lapses may cause the slower responses (e.g., Bertelson & Joffe, 1963; Bills, 1937; Hockey, 1986; Sanders, 1998). The lapses were believed to be involuntary resting pauses, enforced by the accumulation of fatigue during the task (Bertelson & Joffe, 1963; Sanders & Hoogenboom, 1970). This notion was also supported by studies showing that mental fatigue, as induced by prolonged task performance, primarily affects the upper end of the intraindividual RT distribution (Fiske & Rice, 1955; Welford, 1984). In addition, it has been suggested that occasionally occurring task-irrelevant events are often responsible for some of the response time outliers (Jensen, 1992; Smallwood et al., 2004; Ulrich & Miller, 1994), particularly when it is required to maintain performance over extended time periods (Stuss, Meiran, Guzman, Lafleche, & Willmer, 1996; Stuss, Murphy, Binns, & Alexander, 2003).

Recent findings indicate that under conditions requiring higher degrees of response control, increased variability in ADHD is present throughout the RT distribution, regardless of ADHD subtype, reflecting inefficiency in neural mechanisms critical to engaging a state of preparedness to respond (Hervey et al. 2006 ; Castellanos et al. 2005). Children with ADHD, however, do not only have increased RT variances, they also seem to be slower in their mean response times. In many response time tasks, larger mean response times are accompanied by larger response time variances (e.g., Luce, 1986; Wagenmakers & Brown, 2007; Wagenmakers et al., 2005). Most explanations of this phenomenon involve the proposition of an information accumulation process for which this dependence between mean and variance holds naturally (see Luce, 1986; Ratcliff, 1978, Carpenter and Williams 2005; Pouget et al. 2011). For example, a change in information accumulation efficiency then causes a change in mean response times as well as a change in response time variance (Shadlen and Newsome, 1997; Hanes and Schall, 1995; Pouget et al., 2011). Other factors than accumulation efficiency may also influence information processing. Therefore, it is possible that the increased RT variance is, at least partially, due to the same source that causes the overall slower responses.

3. Variability and stationarity

As presented in the preceding paragraphs, the literature supports the view that intra-individual RT variability in sustained attention tasks is an empirical phenomenon distinct from other performance characteristics (Pieters, 1985; Sanders, 1983). It is in fact very compelling that in many RT tasks the observed within-person variability is 20% to 50% of the between-person variability when both are expressed in standard deviation units. In development, an increase with age in intra-individual-variability might be expected if fluctuating levels of performance are an early sign of cognitive decline. It is also possible that, for some variables, higher amounts of intra-individual-variability in elderly persons are positive, rather than negative, outcomes. For example, higher variability might signify greater adaptability, less rigidity, or more creativity. Numerous publications on substantive aspects of the topic (e.g., Butler, Hokanson, & Flynn, 1994; Eizenman, Nesselroade, Featherman, & Rowe, 1997; Hertzog, Dixon, & Hultsch, 1992), treatments of pertinent methodological issues are also appearing with rapidity (e.g., Boker & Nesselroade, 2002; Browne & Nesselroade, 2002; Hamaker, Dolan, & Molenaar, 2003; McArdle, 1982; McArdle

& Hamagami, 2001; Molenaar, 1985; Moskowitz & Hershberger, 2002; Nesselroade & Molenaar, 1999; West & Hepworth, 1991).

Just how important does information on intra-individual variability seem to be in the current state of behavioral inquiry? When intra-individual variability in a given attribute is small, the inter-individual differences in that attribute supply the useful information, from a prediction standpoint; when intra-individual variability is large, however, they may not. Indeed, in the latter case, scores from only one occasion can yield highly misleading inter-individual-differences information. From the perspective of classical theory, short term, intra-individual variability is noise. Opposing such negative sentiments are the more positive findings that short-term intra-individual variability is a valid indicator of substantively important events. But the balance between noise and stationarity is fragile. A source of adaptation in some cases too much variability can also lead to dramatic loss of efficacy. Several pieces of evidence suggest that increased intra-subject variability may be a good candidate as an intermediate endophenotype of ADHD (Castellanos & Tannock, 2002, Castellanos, Sonuga-Barke, Milham, & Tannock, 2006). First, increased variability in responding has been demonstrated to correlate with impulsive responding and self-report of inattention to tasks (Rommelse et al., 2007; Simmonds et al., 2007; Strandburg et al., 1996), suggesting that variability in responding is a contributing factor to expression of diagnostic characteristics of ADHD. Further, several studies have demonstrated that close family members of individuals with ADHD demonstrate increased variability in responding, including, siblings sharing an ADHD diagnosis, discordant dizygotic twins, and siblings who do not meet criteria for diagnosis of ADHD (Bidwell, Willcutt, DeFries, & Pennington, 2007; Rommelse et al., 2007). This pattern of results suggests a genetic mechanism for expression of the phenotype. Analyses characterizing intra-individual variability in ADHD has revealed a pattern of occasional responses with unusually long reaction time, with the majority of responses being comparable to comparison groups (Castellanos et al., 2005; Hervey et al., 2006; Leth-Steensen, King Elbaz, & Douglas, 2000).

4. Neurophysiological substrate of intra-individual variability

Aside the genetic approaches, cognitive and neurophysiological studies have revealed that candidate endophenotypes in ADHD include inhibitory-based executive deficits associated with frontal-striatal dysfunction (Nigg et al 2005) delay-related motivational processes linked to limbic-ventral striatal circuits (Sonuga-Barke 2002, 2003); cerebellar-based timing deficits (Toplak et al 2003); and posterior parietal noradrenergic orienting deficits (van Leeuwen et al 1998). Given the likely pathophysiologic heterogeneity of ADHD, all these candidates are not mutually exclusive; they could each be playing substantial roles in different clusters within the ADHD groups of patients. At a molecular level, dysfunctional modulation of select neurotransmitters, including those in the catecholamine and ACh systems, gives rise to increased neural noise that might contribute to increased intra-individual variability in cognitive performance. Alterations in the dopamine system are well documented in populations that exhibit increased behavioral intra-individual variability, including the elderly, ADHD children (Bellgrove et al. 2005), schizophrenics and patients with Parkinson's disease. These findings have been substantiated in computational modeling studies showing that reduced dopamine activity increases neural noise, resulting

in less distinct cortical representations manifest as decreases in cognitive performance and increases in behavioral intra-individual variability.

At a whole-brain level, functional activation techniques, such as electroencephalograms (EEGs) and functional magnetic resonance imaging (fMRI), are tempting to link behavioral intra-individual variability to brain function. Functional imaging studies in children with ADHD did observe abnormalities in inferior and medial prefrontal, striatal and temporo-parietal brain regions during tasks of interference inhibition (Vaidya et al., 2005; Konrad et al., 2006; Rubia et al., 2007b, 2009c, 2011a; for review see Rubia, 2010). Adults with ADHD when compared to controls in an a priori region of interest, show less activity in anterior cingulate (Bush et al., 1999), while other studies found reduced activation compared to healthy adults in the right inferior prefrontal cortex during event-related interference inhibition trials, but enhanced right medial frontal activation for a blocked interference inhibition condition (Banich et al., 2009). Inconsistent findings of either increased or decreased frontal, parietal, temporal and cingulate activation in adults with ADHD compared to control subjects were also observed in fMRI studies of other executive functions as such motor response inhibition and working memory (Epstein et al., 2007; Banich et al., 2009; Dibbets et al., 2009; Cubillo et al., 2010). The inconsistencies between findings could be related to the fact that most of the published fMRI studies in adult ADHD have included patients with a stimulant medication history (Bush et al., 1999; Valera et al., 2005, 2010a; Hale et al., 2007; Banich et al., 2009; Dibbets et al., 2009; Wolf et al., 2009; Cubillo and Rubia, 2010). Chronic stimulant medication is an important confound given evidence for long-term effects of stimulant medication on brain structure (Bledsoe et al., 2009; Shaw et al., 2009) and function (Konrad et al., 2007 but see Cubillo et al., 2010). But inconsistency could also be related to averaging methods used to analyze these data, while behavioral studies have revealed a critical role in response variability.

Using structural magnetic resonance imaging (MRI) in ADHD patients, recent studies found reduced volume and cortical thickness in inferior prefrontal cortex (IFC) but also other frontal brain regions, as well as parieto-temporal regions, the basal ganglia, the splenium of the corpus callosum, and the cerebellum (McAlonan et al., 2007; Durston et al., 2004; Semrud-Clikeman et al. 2000; Berquin et al. 1998; Mostofsky et al. 1998). Recent analyses of structural data in childhood ADHD have also shown reductions relative to control subjects in posterior inferior vermis of the cerebellum, the splenium of the corpus callosum, total and right cerebral volumes, right caudate, and various frontal regions (Tian et al., 2006). The other meta-analysis was of whole-brain voxel-based morphometry imaging studies, avoiding the a priori bias of region selection, and identified a significant regional gray matter reduction in ADHD children compared with control subjects in right putamen and globus pallidus (Qui et al. 2009; Qiu et al. 2010). Diffusion tensor imaging studies have furthermore provided evidence for abnormalities at the neural network level, showing abnormalities in multiple white matter tracts in cingulate and fronto-striatal, as well as fronto-parietal, fronto-cerebellar, and parieto-occipital white matter tracts, in children, as well as adults, with ADHD compared with comparison subjects (Konrad et al. 2011; Thomason and Thompson 2011; Konrad et al. 2010; Ashtari et al. 2005). Longitudinal imaging studies have provided evidence that the structural abnormalities in these late-developing fronto-striato-cerebellar and frontoparietal systems are due to a late structural

maturation of these regions (Rubia, 2011; Rubia et al. 2009; Yang et al. 2007). Thus, the peak of cortical thickness maturation has been shown to be delayed in children with ADHD compared with healthy peers, including frontal and temporal areas (Shaw et al. 2009; Shaw et al. 2007; Durston et al. 2003). All these regions and connections could be part of a network responsible for the variability and stationarity of behaviors, and particular defects on these networks could result in the observed and pathological expression of ADHD.

Finally and to go back to the first describe genetic approach. A strong genetic contribution to ADHD was evidenced through twin, family and adoption studies, and considerable efforts have been made to identify genes involved in its etiology (for recent review see Cummins et al. 2011; Finke et al. 2011; Semrud-Clikeman et al. 2011). However, results of candidate gene associations for ADHD yielded largely inconsistent results. Dopamine dysregulation is thought to play a crucial role and the dopamine genotypes of DAT1 and dopamine receptor D4 (DRD4) 7-repeat allele are most commonly associated with the disorder (Johnson et al. 2008). The DRD4-7-7 genotype has been associated with reduced volume and cortical thickness of the right IFC in normal development, which was, furthermore, particularly pronounced in ADHD children with the genotype (Semrud-Clikeman et al. 2011). The DAT1 genotypes have been associated with abnormal caudate volume, as well as activation in patients with ADHD (Tovo-Rodrigues et al. 2011; Szobot et al. 2011; Todd et al. 2005). Antisocial behaviors, including psychopathy, have more commonly been associated with serotonin genotypes. Thus, the short allele of the serotonin transporter has been associated with impulsive and antisocial behavior features in alcohol abuse (Li et al. 2010; Herman et al. 2011, see also for review Nordquist and Orelund, 2010) in adults. In healthy adults, it has been related to a dysmorphology and dysregulation of the ventromedial prefrontal cortex, including anterior cingulate and medial frontal cortex, and the amygdala, as well as the functional connectivity between both structures. Abnormal connectivity between amygdala hyperactivity and orbitofrontal hypo-responsivity in relation to negative emotions has been suggested to underlie impulsive aggression (Rubia et al. 2011). Genetic predisposition, hence, may play a role in the development of the disorder-specific dysregulation of IFC-striatal and ventromedial-limbic neural networks in ADHD and antisocial-aggressive behaviors, respectively.

There are still a great number of methodological questions that remain to be addressed in the field of behavior intra-variability. Moment-by-moment fluctuations characteristic of biological processes are fundamentally dynamic in that their quantity and quality of patterning and periodicity are highly sensitive to contextual factors (Stein and Kleiger 1999). However, in many cases, variability is handled by collapsing across time intervals, yielding a single-point estimate of deviation around the mean (SD) for each subject. Group comparisons of variability are then based on group means of individual SD. Thus, although RT studies in ADHD are nearly too numerous to count, the question of the robustness of the association between ADHD and variability has yet to be addressed quantitatively. Significant factors, such as the context within which the organism is working, the tasks being performed, and the internal physiologic and/or cognitive state are affecting intra-individual variability (Borger and Van der Meere 2000; Leung et al 2000; Sonuga-Barke 2003; Swaab-Barneveld et al 2000). For this reason, an analysis of the dynamic properties of ISV requires an examination of the extent to which it is both modifiable and modified by

changes in contextual factors. Indeed, intra-individual variability might be distinctive not only in terms of amount or degree and its temporal structure and periodicity but also in terms of its relationship to other factors within the environment, as demonstrated by the frequently documented observation that the performance of children with ADHD is highly context dependent (Corkum and Siegel 1993). To address this issue, one needs to study the quantitative and qualitative characteristics of intra-individual variability in diverse physiologic states. More systematic investigation of the nature of intra-individual-variability and change in a wide array of attributes is both compelling and timely. The first aspect on which, one needs to focus the methodological and the relevant evaluation of the representativeness of single-occasion assessment. The second aspect relates to whether there are age differences in moment-to-moment, or day-to-day, intra-individual-variability and, if so, what are their salient features.

5. Discussion

Just how important does information on intra-individual-variability seem to be in the current state of behavioral inquiry of ADHD? In the last decades, it has been argued that increased intra-individual-variability in cognitive performance could indeed be a valid indicator of impending cognitive change in children (Eizenman et al. 1997; Rowe and Kahn, 1987; Castelanos et al., 2002). However even more systematic investigation of the nature of intra-individual variability and change in a wide array of attributes is both compelling and timely.

These examinations will be necessary for at least two reasons. To better understand the interactions between three key notions of stability, variability, and adaptability; but also to assess at a statistical and functional levels the normal and pathological dynamics of a given system and its behavior over time. Indeed, understanding the relationship between these concepts constitutes a key issue in research on complex biological systems in fields like human motor control and performance. Stability can be specified either by the property of a system to resist changes, that is, to exhibit minimal variation while facing changing conditions, or by its ability to recover a state of equilibrium after perturbation. This may be contrasted with a dynamic form of stability, which refers to reproducible and predictable *patterns of changes* in the system's functioning under varying internal or external constraints. While static stability implies that the variables determining the system's state are maintained within a limited range, the dynamic definition allows the stability of some global behavior to be maintained by changing states of the system (Ahn, Tewari, Poon, & Phillips, 2006).

A general assumption is that enhanced variability of a given behavior reflects its reduced stability. Therefore, behavioral stability has often been appropriately inferred from the observation of small variance. However, even though stability and variability (as assessed by basic Gaussian statistics) are obviously two related aspects, the invariant nature of this relationship is arguable. One may intuitively wonder, for instance, which of the following two behaviors should be termed "more stable": the behavior that exhibits the smallest fluctuations or the behavior that is perpetuated *in spite of* maximal variability (Riley & Turvey, 2002). In other words and to go back the title of our chapter one may question the

origins of the fragile balance between variability, noise and predictability in control of human behavior.

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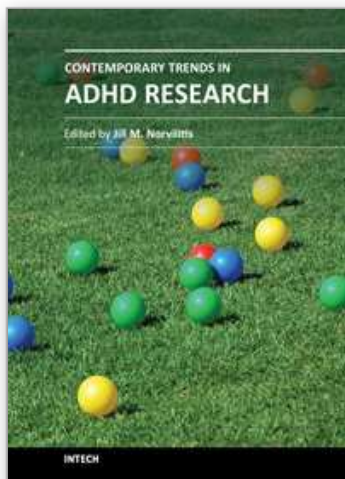
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With many children and adults affected by Attention Deficit Hyperactivity Disorder, researchers strive to understand the underpinnings of ADHD and associated factors on both a basic and applied level. The goal of this volume is to explore some of the broad array of research in the field of ADHD. The 12 chapters cover a variety of topics as varied as postural control, endocrine dysfunction, juvenile justice, and academic outcomes. These chapters will provide valuable insights for students reading about ADHD for the first time, researchers wishing to learn about the latest advances, and practitioners seeking new insight in the field.

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