

# The patient as a moving target: the importance to rehabilitation of understanding variability

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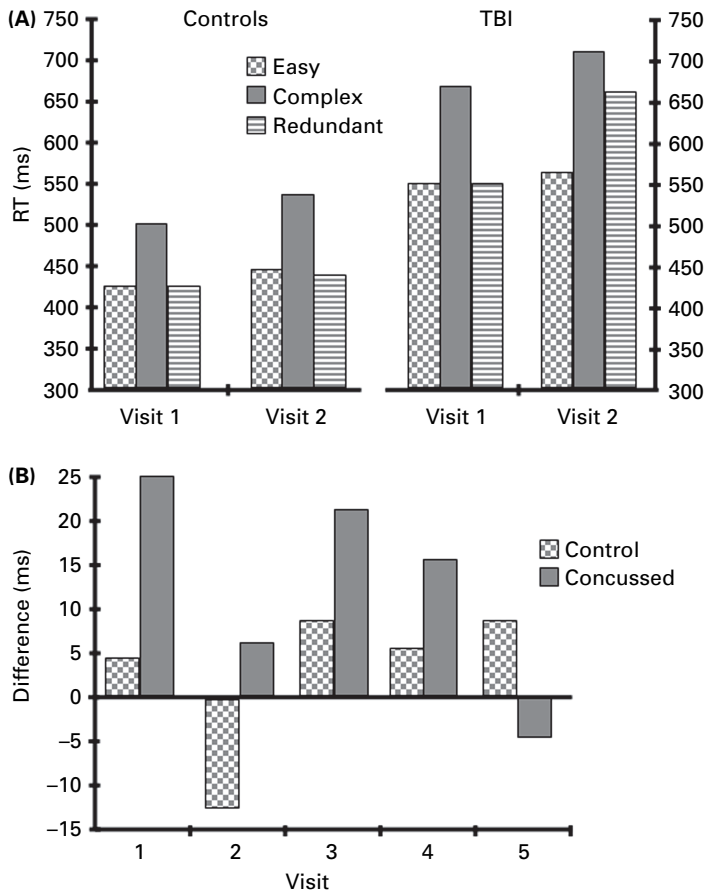
## Introduction

- In the history of understanding human behavior, there has been conflict between two different research approaches: the study of group effects versus the examination of individual differences, more generally described as central tendency versus variability in performance.
- Understanding variability may be key to accurate diagnosis and treatment.
- There are five sections to the chapter: Introduction, Definitions and measurements of variability, Factors affecting intra-individual variability, Potential mechanisms underlying variability and Clinical implications.

The efficacy of rehabilitation depends on several issues, not the least of which is the understanding (and by implication measurement) of fundamental principles of human behavior. This in turn would seem to imply a certain level of consistency of such behavior. The history of psychology reflects this premise. Despite observations by early psychologists of “performance oscillations” during the completion of different tasks (e.g., Flugel, 1928; Hull, 1943; Philpott, 1933 – see Barratt, 1963; Jensen, 1992, for a historical background), the goal of cognitive research eventually became focused on central group tendency (Cronbach, 1957; Surwillo, 1975). Variability was viewed as a nuisance, which was managed by testing more subjects and by averaging scores (Cronbach, 1957; Jensen, 1992). Yet central tendency does not provide the full range of information. In reaction time (RT) tasks, for

example, the distribution is often skewed. Maximum speed of response may be physiologically limited, but slowing is not, resulting in a long right tail as slow responses are more broadly distributed (Logan, 1992; Ulrich & Miller, 1994; Wagenmakers *et al.*, 2005). The inability of a patient to perform a task in a stable manner would appear to be a major impediment to the benefit one obtains from rehabilitation, and would influence his/her ability to transform what they might have learned in rehabilitation to the demands of daily life.

Our first encounter with the problem of variability occurred during a study that attempted to answer the question (e.g., van Zomeren, 1981) of whether there was a focused attention deficit after moderate to severe traumatic brain injury (TBI). Patients were tested twice, one week apart, in an effort to demonstrate the replicability of the effect (Stuss *et al.*, 1989, 1994c). The TBI patients were slow, as expected – but a review of the results of the first week unveiled no evidence of a focused attentional deficit. Analysis of the second week’s results, on the other hand, indicated the same slowness, but now there was evidence of the expected focused attention impairment. The data were obviously not replicable, and were going to be rejected. Fortunately, the data from a second study on the recovery from mild concussion (testing patients five times over a 3-month period) completed at the same time showed a similar, albeit milder, inconsistency of performance (see Figure 3.1). A third factor supported the conclusion that variability was not a nuisance but an important observation – the results



**Figure 3.1.** Performance on correct trials in all three conditions (Easy, Complex, Redundant) of the Multiple Choice Reaction Time Task: Easy – response to one simple target and three distractors; Complex – target defined by three features (color, form, and shading), with all distractors sharing zero, one, or two features with the target; Redundant – target defined by three features, but the distractors share no features with the target. The target appeared with a probability of 0.25. The Redundant condition was hypothesized to index focused attention since the demands were equivalent to the Easy condition, but the target was visually equivalent to the Complex condition.

(A) The top part of the figure illustrates response time (RT) to correct target responses for all three conditions over two test sessions one week apart. Control participants are on the left, and the patients are on the right. On the first visit, the traumatic brain injured (TBI) patients were slower but the pattern of responses across all three conditions paralleled those of the Control participants. On the second visit, the TBI patients, in addition to slowness, demonstrated a focused attention impairment as shown in their poor performance in the Redundant condition compared with the Easy condition. Reprinted with permission from Stuss *et al.* (1989).

(B) The bottom half of the figure depicts the performance of mildly concussed patients over five visits. The dependent measurement in this figure is the difference in RT between the Redundant and Easy conditions. The Concussed patients were more variable in their focused attention performance across five visits over a 3-month period compared with matched Control participants. Reprinted with permission from Stuss & Gow (1992).

were consonant with clinical experience. Although patients did not indicate a problem with stability of performance, they often complained about their inability to “stay on the job.” Thus, although central tendency is important, these observations clearly indicated that individual differences and differences *within* individuals are also important, both theoretically and clinically.

The overall objective of this chapter is to highlight the importance of variability of performance. Specific aims, divided into the major sections of the chapter, are to provide a handy glossary of different types of variability and ways to measure these; to understand what external and internal factors might impact variability; and to examine possible etiological mechanisms, as these might be the key to successful treatment and management of variability. There is little published on actual rehabilitation of variability. We end the chapter with a section on clinical implications, including case studies, that suggest how this knowledge might be implemented in cognitive rehabilitation.

### Definitions and measurements of variability

Variability can exist within an individual and between individuals in a group and both play an important role in research trying to understand brain-behavior relations. Minimising group variability is likely a key first step in the study of rehabilitation efficacy. The emphasis in this chapter is on the within- or intra-individual variability, since this type may have a particularly significant impact on clinical rehabilitation, and the outcome of rehabilitation trials.

Central tendency indexes core ability; variability assesses change. It has been claimed that the study of variability within an individual is the best technique to analyse change (Nesselrode, 1991). Changes that influence performance can be long-term or short-term. Longer-term change is more durable and systematic, as seen, for example, in personality traits. The focus in this chapter is on shorter rapid fluctuations that are more or less reversible. For

each type of variability, an operational definition is presented, followed by methods of measurement.

- Measurement of variability is key to assessing change.
- Understanding and minimizing between (inter) individual variability is the first step in assessing brain-behavior relations, including the relation of variability to different brain regions or disorders. This diversity of performance can be measured, for example, by the standard deviation of individuals' scores around the mean of the group.
- There are three general types of within (intra) individual variability which we call dispersion, inconsistency and scatter.
- Dispersion is the intra-individual variation of performance across trials within a single task. Dispersion can be measured, for example, by the standard deviation of a subject's observed values within a single test at a single session.
- Inconsistency is the intra-individual variability of performance across different testing sessions. It can be measured, for example, by the standard deviation of an individual's observed values on a given test across several testing sessions.
- Scatter is the intra-individual variability of performance across different tests. It can be measured, for example, by the standard deviation of an individual's observed scaled scores on several tests which perhaps each cover different cognitive domains.

### Inter-individual variability

#### *Background*

Group variability is defined as differences between individuals (*inter*-individual) performing the same task. Following Hale *et al.* (1988), this inter-individual (sometimes called “between person”) variability is labeled diversity (Stuss *et al.*, 1994c, 2003; see also Hultsch & McDonald, 2004; Hultsch *et al.*, 2002; Williams *et al.*, 2005).

Individual differences are normal, and will naturally result in some group variability. The key question is – how much inter-individual variability is reasonable

for a defined group? If the group is inadequately defined as might occur if specific factors are not controlled, we may be inflating diversity. As a consequence, inflated variance may obscure statistical evaluation of differences between groups. Our research into the functions of the frontal lobes highlights the importance of this question. For example, studies of memory dysfunction after frontal lobe damage led initially to the conclusion that frontal lobe damage did not result in a recognition memory deficit (Janowsky *et al.*, 1989). However, upon further specification within the frontal lobes, it was clear that damage to specific regions of the frontal lobes did result in a significant recognition deficit (Alexander *et al.*, 2003; Stuss *et al.*, 1994a). A meta-analysis confirmed that this result was obscured by the way frontal groups were defined (Wheeler *et al.*, 1995). That is, in initial studies, “frontal groups” were too broadly defined. When defined more precisely (e.g., in more refined anatomical subgroups, or by controlling for different factors such as depression), group studies can yield important results in the presence of non inflated inter-individual differences (Drai & Grodzinsky, 2006a, 2006b).

### *Methods*

Various techniques have been used to reduce heterogeneity in a group of individuals by constructing new groups that make anatomical and/or behavioral sense. As a general approach in lesion studies, we have conceptualized performance on a given test as an independent variable and lesion location as a dependent variable. One technique, following this general conceptualization, involves overlapping shadows of lesion-extent of individuals who have impaired performance compared with control subjects (e.g., Shammi & Stuss, 1999). Those areas that show a high degree of overlap are considered to be potentially influential in performance of the task. A confounding factor may occur if a non-task-related brain area is lesioned in all of the patients; then a high degree of overlap will be seen at this location among those patients who are impaired on a task.

A modification of the overlapping lesions approach, with a nod to functional neuroimaging’s statistical parametric map, involves statistically quantifying the association between presence or absence of damage within defined architectonic regions (e.g., Petrides & Pandya, 1994) and performance (Alexander *et al.*, 2005; Picton *et al.*, 2006; Rorden & Karnath, 2004; Stuss *et al.*, 2005). By comparing performance of patients with damage in a given location to performance of patients without damage in that area, this architectonic localization (or “hotspot”) analysis does not suffer from confounding with frequency of lesion occurrence.

As an alternative to identifying patients with abnormal performance, patients’ performance can be classified using a median-split partition (Stuss *et al.*, 1994a). That is, undertaking a performance-based division of a set of patients into two subsets of equal size based on their performance as a first step in examining the anatomical or behavioral factors that are relevant to performance. Then, frequency of abnormality in defined anatomical regions can be investigated with respect to these performance-based subsets (Stuss *et al.*, 2001a).

Identification of more homogenous groups demonstrates that diversity may not be simply realizations of random error, but may be related to a combination of one or more relevant factors. This was demonstrated in a study of the recovery of continuous memory after traumatic head injury. When patients were initially grouped by a standard injury severity measure, considerable heterogeneity in recovery time of post-traumatic amnesia was observed (Stuss *et al.*, 2000a). Using the Classification and Regression Tree method (CART; Brieman *et al.*, 1984) and incorporating multiple variables (e.g., demographic information such as the age of the patient; multiple injury severity measures), we were able to meaningfully reduce variability of observed recovery time intervals (see also Temkin *et al.*, 1995).

The importance of deriving a more finely grained partition of patients has been demonstrated in multiple group studies (e.g., Aron *et al.*, 2003; Bechara *et al.*, 1998; Bigler *et al.*, 1994; Damasio & Damasio,

1989; Fellows & Farah, 2005; Godefroy *et al.*, 1998; Godefroy & Rousseaux, 1996; Hornak *et al.*, 2004; Richer & Boulet, 1999; Simons *et al.*, 2005; Tranel *et al.*, 2002). There is obvious application to rehabilitation. Negative findings in group studies may be secondary to group diversity, resulting from inadequate specification of groups. If all individuals in a defined research group do not respond to a given rehabilitation approach and the statistical comparison is negative, the cause may be group constitution and not the efficacy of the rehabilitation.

### Intra-individual variability

#### *Background*

Intra-individual variability (IIV) (Barratt, 1963) (also termed within-subject, or within-individual, variability) can be exhibited over a spectrum of time scales. At the relatively short-term end of this spectrum – described as “moment to moment” variability (Rabbitt *et al.*, 2001) – are brief inter-observation time intervals such as those associated with millisecond-level sampling rates of neuroelectric signals and minute-level reaction time trials. At the longer-term end of this spectrum – generalized as “day to day” variability (Rabbitt *et al.*, 2001) – are longer time frames such as daily, monthly, or potentially yearly testing sessions. This spectrum suggests categorization of variability at different temporal resolutions.

From a practical perspective the “moment to moment” end of the IIV spectrum can be defined operationally as variability across trials within a continuous testing session (Rabbitt *et al.*, 2001; Stuss *et al.*, 1994c, 2003). The “day to day” end of the spectrum may be operationally defined as intra-individual variation between different testing occasions (Rabbitt 2001 – “between session” variability; Stuss *et al.* 1994c, 2003). In this chapter, these two types of IIV are referred to as *dispersion* (between trials) and *inconsistency* (between sessions), and are discussed below. Not only is it operationally appealing to separate IIV into between-trial and between-session classifications, but this partition

also appears to characterize distinct behavioral facets (Hultsch *et al.*, 2000; Rabbitt *et al.*, 2001; Shammi *et al.*, 1998; see discussion later in this chapter).

Operational definitions of these terms vary among research groups and care should be taken when comparing different papers. Rabbit and colleagues use the term “within session” variability; we use the term “dispersion.” Dispersion has also been defined (Hultsch *et al.*, 2002) as the variability of an individual across different tasks tested at a single session (which we define as scatter). The term inconsistency has elsewhere been used to encompass both dispersion and inconsistency: “within person variability in performance on a single task measured on multiple occasions, either across testing sessions, or across separate trials within the same testing session” (Williams *et al.*, 2005, p. 88).

Differences between an individual’s scores across tests assessing different cognitive domains, but with numerically comparable scales, can be a useful measure in the analysis of behavioral status. The term “scatter” has been used to describe this variation of an individual’s performance on different tests (Matarazzo *et al.*, 1988; Schretlen *et al.*, 2003). Not yet investigated, but a potential area for future research, is the overlap between scatter and dispersion, since different tests (or subscales) are typically evaluated over a substantive interval of time allowing cumulative short-term fluctuations (dispersion) to be exhibited.

### Methods

The distinction between predictable variability based on a set of factors and variability that is generated by chance is relevant theoretically and clinically. While we are not suggesting that the factors implicated in predictable variability are easily identifiable or measurable, it is important to investigate these possible sources of variability (such as practice, fatigue, materials and time-of-day effects) as thoroughly as possible so that they are not aggregated into measures of chance-related variability. In this section we present methods of quantifying IIV. Some of the following subheadings address

identification of predictable variability (e.g., serial correlation) while others present summary measures of IIV (e.g., coefficient of variation).

### *Standard deviation*

A reasonable measure of the spread of a set of observations is the expected distance between an observation and the center of the distribution of observations. If we allow the center of the distribution to be represented by the average of the observations, then we can compute the sample variance ( $s^2$ ) as an average of the squared distances:

$$s^2 = \frac{\sum_{i=1}^n (x_i - \bar{x})^2}{n - 1}$$

where  $n$  is the size of the sample. Note that degrees of freedom ( $n - 1$ ) is used in the denominator instead of the sample size ( $n$ ) in order to obtain an unbiased estimate of the population variance. The sample standard deviation ( $s$ ) is the square root of the sample variance and has the same units as the observations. The standard deviation of a sample of observations from an individual person is sometimes referred to as the individual standard deviation (ISD).

### *Coefficient of variation*

There are empirical and theoretical reasons for being alert to the possibility that the variance of a variable may be related to its mean. Response time studies, for example, have reported a relationship between location and spread of latency performance (e.g., Jensen, 1992) and many of the distributions that provide a good description of response time data yoke mean and variance together (more on this in the discussion of response time distributions, below). One statistic that attempts to accommodate a relationship between mean and variance in a straightforward manner is the coefficient of variation. The coefficient of variation is defined as the standard deviation divided by the mean. This statistic assumes a constant unitary relationship between mean and standard deviation.

### *Serial correlation*

Given a series of observations on a given individual, it is often expected that there will be an association between consecutive observations and even perhaps between observations that are separated by a given lag. Slifkin & Newell (1998) highlight a couple of methods for describing serial correlation: empirical autocorrelation as a function of lag and approximate entropy which measures the degree of predictability between two sections of a series of observations – see Pincus (1991).

A simple way to visually inspect lag-1 autocorrelation in an observed series is with a scatterplot of the value of each observation ( $t + 1$ ) versus the value of the immediately preceding observation ( $t$ ). The sample lag-1 autocorrelation coefficient may be calculated as follows (Wei, 1990):

$$r_{\text{lag-1}} = \frac{\sum_{t=1}^{n-1} (x_t - \bar{x})(x_{t+1} - \bar{x})}{\sum_{t=1}^n (x_t - \bar{x})^2}$$

Note that the standard correlation coefficient calculated between two variables in which one is the same as the first but with the observations shifted by one position is not exactly the same as the sample lag-1 autocorrelation for a finite sample size. Lag-1 autocorrelation provides an index of the predictability of the value of the subsequent observation based on the current observation.

### *Non-stationarity*

A (covariance) stationary series of observations has constant mean and variance across time (Wei, 1990). For series which are not stationary in this sense, it is important to accommodate sources of non-stationarity prior to evaluating measures of IIV. Sources of non-stationarity in a series of trial-to-trial observations might include fatigue and practice effects.

If a subject's performance changes (or drifts) linearly over time, for example, then the series is not stationary. Linear regression might be used to accommodate consistently changing performance over time. This change in performance could be

seen as theoretically separable from random moment to moment variability and should be excluded from the determination of finer resolution variability.

### *Outlying observations*

Examination of observations with extremely small or large values can be a useful step in verifying that erroneous observations are not being included in the statistical analysis of observed data. While it may seem appealing to simply adhere to a rule of thumb such as rejecting values that fall more than three standard deviations away from the mean, there are various arguments against its application. First, although such an observation may be uncommon, it is not necessarily erroneous. It is expected that about 1 in 526 observations on a random variable with a symmetric normal distribution would exceed the mean by three standard deviations or more. To put this ratio into a context, 1 in 529 people in Canada were 93 years of age or older in 2001. While it may be uncommon to run across someone who is 93 years old or more, you would not want to exclude them from a summary of the population's age distribution.

It is also possible that an observation falling three standard deviations away from the mean is not even uncommon. Consider, for example, a variable with skewed distribution. About 1 in 55 observations on a random variable with an exponential distribution would be expected to exceed the mean by more than three standard deviations. Rather than excluding such an observation it would be more sensible to identify a more appropriate distribution upon which to base characterization of the observed values. The ex-Gaussian distribution, for example, has been used successfully to model long tails often found in response time data (see below).

A method for identifying a threshold below which response time observations might be considered to be generated by a process other than the one under study was described by Ratcliff & Tuerlinckx (2002). This method examines fast trials and sets a threshold at the response latency for which accuracy

crosses chance performance. Identifying contaminant observations is described as a critical step since they could inappropriately influence estimation of parameters used to describe the process of interest. In general, this is the important criteria. Observations should not be identified as outlying based on statistics alone but must incorporate information regarding the processes involved in generating the observation.

### *Response time distributions*

Response time tasks are a popular way to study intra-individual variability. Much has been written about statistical distributions which may be motivated by models of mechanisms underlying task performance, or may simply fit observed response time data well. Pertinent to the discussion of variability, these distributions provide an intrinsic association between the mean and variance of the random variable. Both the lognormal (Ulrich & Miller, 1994) and the Weibull (Logan, 1992) distributions, for example, have been found to fit empirical response time data well and can be motivated by models of response time task performance. Both lognormal and Weibull distributions are specified by shape and scale parameters and their means and variances are functions of both parameters. Changing either of these parameters affects both mean and the variance. Wagenmakers and Brown review commonly used response time distributions and examine empirical evidence regarding the relationship between the mean and standard deviation of response time (Wagenmakers & Brown, 2007).

### *Ex-Gaussian distribution*

The ex-Gaussian distribution is the convolution of the one-parameter exponential distribution and the two-parameter normal (or Gaussian) distribution. Specific aspects of the shape of the distribution may be summarized by each of the three ex-Gaussian parameters which index the location ( $\mu$ ) and scale ( $\sigma$ ) of the normal distribution and the scale of the exponential distribution ( $\tau$ ). This

distribution has been used to model response time data (e.g., Heathcote *et al.*, 1991; Ratcliff & Murdock 1976; West *et al.*, 2002). Estimates of the parameter values may be obtained by various techniques. Van Zandt (2000) assessed six of the more commonly used estimation techniques and found that maximum likelihood estimation on the whole sample recovered parameters with least bias and variability. From a technical perspective, it should be noted that the range of the ex-Gaussian distribution extends into negative numbers which is not generally the case for response time observations – a discrepancy which is typically overlooked in practice.

While the variance of an ex-Gaussian random variable is a function of two scale parameters,  $\sigma$  and  $\tau$ , it has been argued that analysis of estimates of these separate parameters can be more appropriate than analysis of the sample variance since the effect of manipulated factors on the variance of a distribution of observations could be exhibited either through the general spread of the distribution or by specific changes in the right hand tail (Heathcote *et al.*, 1991). For example, Hultsch and colleagues (2002) found age differences in IIV to be larger for the slowest 20% of an individual's responses.

### *Scatter*

Three indices of scatter were suggested by Matarazzo *et al.* (1988) and were applied to scaled scores for the 11 subscales of the WAIS-R. For an individual's set of observed values on different tests, the range (maximum value minus minimum value) and the standard deviation (both standard measures of spread) may be calculated as indices of scatter. The third proposed index was the number of observed values for a given individual that exceed subject-specific upper and lower thresholds. Thresholds were defined as those beyond which observed values were significantly different from the subject's mean scaled scores. Maximum deviation (Schretlen *et al.*, 2003) is another statistic that has been used to measure scatter.

Mahalanobis distance is a measure of distance of a multivariate observation from the center of a population. This measure has been described as a useful

measure of scatter for measures such as the Wechsler Intelligence Scales (Burgess, 1991) because it is more sensitive to discrepancy between strongly correlated subscales than between weakly correlated subscales.

### **Factors affecting intra-individual variability**

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Exogenous and endogenous factors may affect IIV. These include task demands, situational factors, normal population factors, neurological conditions and neuropsychiatric disorders.

- Assessment of IIV, and awareness of IIV in rehabilitation, necessitates the awareness of the context during the assessment.
- Task factors, such as difficulty and type, play an important role.
- Situational factors can significantly affect IIV. Factors to consider are fatigue, diurnal rhythms, sleep loss, psychosocial factors, test practice and method of administration.
- Population factors may have substantial impact on IIV, with level of intelligence and age having been most commonly investigated.
- Many neurological disorders have been associated with greater intra-individual variability: mild cognitive impairment, dementia of various types (Alzheimer's, Parkinson's, frontal-temporal lobar degeneration), traumatic brain injury and focal brain damage.
- Severity of disease and type of neurological disorder appear to impact IIV.
- Research on focal brain damage suggests that the frontal lobes and cerebellum are two key areas in a system related to consistency of performance. The role of the basal ganglia in this circuit is still controversial and recent evidence suggests that this region does not play a direct role in temporal processing.
- Different regions of the frontal lobes are related to IIV (see control mechanisms in "Neurological disorders" later in this chapter).
- Schizophrenia causes increased IIV.
- Different factors affecting IIV can interact.

### Task factors

Change must be understood in “context;” i.e., those factors which influence change (Cronbach, 1957; Parasuraman, 1976). Task difficulty is an important factor which increases variability. This appears to be true for most populations, but may be particularly relevant in vulnerable populations. This vulnerability has been demonstrated in the elderly (Bunce *et al.*, 2004; Cerella, 1985; Salthouse, 1985, 1992; Shammi *et al.*, 1998; West *et al.*, 2002) and patients with Parkinson’s disease (Perbal *et al.*, 2005). The type of task is also relevant, although this factor may well be difficult to dissociate from task difficulty. Increased variability was found in reproduction of timed intervals by Parkinson patients, but not in production of timed intervals (Perbal *et al.*, 2005). Different tasks may elicit IIV differently. For example, three different types of tasks (reasoning, memory, and perceptual speed) were administered to older adults twice a day over 60 consecutive days (Allaire & Marsiske, 2005). Intra-individual variation was not strongly correlated among task pairs but was among pairs of days within task.

It may not be task difficulty or the superficial task characteristics per se that impact IIV as much as the fact that different tasks affect separate timing systems in the brain (Lewis & Miall, 2003). In such cases, the different timing systems may stress brain regions that are less efficient in a particular population. Lewis & Miall (2003) argue that there are at least two systems, one more automatic and related to motor and premotor circuits, and perhaps involved with the cerebellum; there is also a cognitively controlled system, more dependent on prefrontal and parietal cortices.

### Situational factors

As might be imagined, there are many situational factors that influence variability of performance: extended work periods and excessive fatigue (Bunce *et al.*, 2004; Henning *et al.*, 1989; Hockey, 1983; Sanders, 1998; see Grady, Chapter 9, this volume); sleep loss (Maruff *et al.*, 2005); psychosocial

factors and related physiological measures such as blood pressure (Ong & Allaire, 2005); and alcohol use (Maruff *et al.*, 2005).

Several situational factors deserve more attention because of the direct clinical application. Diurnal rhythms appear to impact variability (Hockey, 1983; optimal time of day – Murphy *et al.*, 2007), although Rabbitt and colleagues (2001) have argued that both within-session variability (dispersion) and between-session variability (inconsistency) are independent of circadian variability unless you do not take into account IQ differences. Both types of IIV have been observed to be separable from practice effects (Rabbitt *et al.*, 2001), although some tasks show that IIV can be reduced with extended practice (Hofland *et al.*, 1981; Ram *et al.*, 2005). The way a test is administered is also important. In the elderly, power (untimed) testing reduces IIV (Hofland *et al.*, 1981). In patient studies, medication has been found to influence performance (Perbal *et al.*, 2005).

### Population factors

Population factors might be considered more endogenous and not driven by exogenous factors. Intelligence and level of education (Christensen *et al.*, 2005; Ram *et al.*, 2005) have been associated with greater variability; lower IQ and less education associated with greater IIV. This has been reported in mentally retarded individuals (Baumeister & Kellas, 1968), the general population (Larson & Alderton, 1990), and in older adults between ages 60 and 80 years, although the effect of intelligence held regardless of age (Rabbitt *et al.*, 2001). Personality variables themselves appear to contribute to variability, at least at the level of neuroticism (Moskowitz & Zuroff, 2005; Robinson & Tamir, 2005).

Perhaps the population variable that most commonly affects both dispersion and inconsistency is age. In general, older adults are more variable than younger adults (Bunce *et al.*, 2004; Fozard *et al.*, 1994; Friedman, 2003; Hultsch *et al.*, 2002; Li & Lindenberger, 1999; Li *et al.*, 2000; Nesselroade & Salthouse, 2004; Rakitin *et al.*, 2005; Salthouse, 1993;

see Morse, 1993, for a meta-analysis comparing the effects of age on IIV across a number of tasks), although task demands may well play a role in demonstrating this (Anstey *et al.*, 2005; Shammi *et al.*, 1998; West *et al.*, 2002;). Not all tasks result in increased IIV with age (Foster *et al.*, 1995). Although mean speed of response is often associated with IIV (Fozard *et al.*, 1994), it is not necessarily so (Hetherington *et al.*, 1996; Segalowitz *et al.*, 1997; Shammi *et al.*, 1998; Stuss *et al.*, 2003).

### **Neurological disorders**

Increased IIV has been reported in children with different disorders (Rovet & Hepworth, 2001; Zahn *et al.*, 1991). Children with attention deficit hyperactivity disorder (ADHD) have higher IIV than control participants, even though there may be no significant differences in average speed of response (Castellanos *et al.*, 2005; Douglas, 1999; Leth-Steensen *et al.*, 2000; Ridderinkhof *et al.*, 2005).

Studies of IIV in adults with neurological disorders can be divided into studies of progressive neurodegenerative disease and acquired focal brain damage. As a general observation in progressive neurodegenerative disease, even mild dementia results in higher IIV than in healthy adults or even those with arthritis, suggesting that this increased IIV is neurological in etiology, and not secondary to general health problems (Hultsch *et al.*, 2000; Strauss *et al.*, 2002). This is true (for at least some abilities) even for mild cognitive impairment (Christensen *et al.*, 2005). In centenarians, inconsistency (between-session variability) was a better predictor of eventual cognitive decline than measures at a single assessment (Kliegel & Sliwinski, 2004).

As might be expected, patients with Alzheimer's disease also exhibit greater IIV than controls (Burton *et al.*, 2006; Duchek *et al.*, 1994). Severity and type of disease have to be considered separately. In a comparison of patients with Alzheimer's and patients with Parkinson's disease (Burton *et al.*, 2006), IIV was related to the severity of the disease process independently of the type of disease. The nature of the disorder also played a role, with

Alzheimer's patients exhibiting more IIV than those with Parkinson's disease. The effect of the type of neurodegenerative disorder, likely reflecting the anatomical systems affected and the clinical symptomatology, is also seen in other comparisons. Ballard *et al.* (2001) found that patients with Alzheimer's disease or Lewy body disease were both more variable than normal elderly individuals, but the IIV was more marked in those with Lewy body disease. A more extended comparison was conducted with the addition of patients who had vascular dementia (Walker *et al.*, 2000). They examined levels of fluctuating consciousness, and found it greatest in Lewy body disease, second largest with vascular dementia, and smallest in those with Alzheimer's disease. In a comparison of patients with Alzheimer's disease and those with frontal-temporal lobar degeneration (Murtha *et al.*, 2002), the latter were more variable, explained by the fact that there was more frontal lobe pathology in frontal-temporal lobar degeneration (see below for focal lesion research).

Research on IIV in Parkinson's disease has been relatively plentiful because of the suggestion that these patients have impaired temporal processing. Several studies reported greater variability of performance in Parkinson patients (Artieda *et al.*, 1992; Harrington *et al.*, 1998a; O'Boyle *et al.*, 1996; Perbal *et al.*, 2005; Rammsayer & Classen, 1997). In other studies, there was no such evidence of increased IIV associated with the disease (Duchek *et al.*, 1994; Spencer & Ivry, 2005). Task factors may play a role, as might the question of medication (Perbal *et al.*, 2005). These data suggest caution in interpreting the relationship of diseases that have more widespread anatomical and neurochemical involvement to IIV. Focal lesion studies may be required to help address the controversy.

Traumatic brain injury (TBI) is an excellent example of the importance of understanding and applying knowledge of the different types of variability. As already noted, multiple factors might determine the nature of particular TBI groups, and using this information for clinical purposes such as prediction requires minimizing group variability (Stuss *et al.*,

2000a). Traumatic brain injury is now known to cause both dispersion (Benton & Blackburn, 1957; Bruhn & Parsons, 1971, 1977; Goldstein, 1942; Segalowitz *et al.*, 1997; Spikman *et al.*, 1996; Stuss *et al.*, 1994c; Whyte *et al.*, 1995; Zahn & Mirsky, 1999) and inconsistency (Stuss *et al.*, 1989, 1994a). Intra-individual variability is observed after both more severe and mild TBI, with some proportional relation to the severity of the injury (Bleiberg *et al.*, 1998; Collins & Long, 1996; Stuss *et al.*, 1994c).

A prominent position about IIV, derived to a great degree from functional imaging research, argues for a cortico striatal network involved in timing and variability (Coull *et al.*, 2004; Macar *et al.*, 2002). Studies in patients with focal brain damage, in particular stroke, are therefore key in investigating which nodes in such a network are necessarily involved in consistent behavior. The example of Parkinson's disease is most telling. As noted, damage of various types that involve the basal ganglia have been reported as resulting in impairment in temporal processing, often associated with IIV (Harrington & Haaland, 1999; Harrington *et al.*, 1998a, 1998b; Macar *et al.*, 2002; Rammsayer & Classen, 1997). However, if only patients with unilateral stroke were examined, deficits were found in motor force control but not increased variability in timing for central or motor implementation (Aparicio *et al.*, 2005). The problems may be more related to changes in other regions or systems, or the interaction of these, with the basal ganglia.

In our first studies on TBI and variability, we had hypothesized that a top-down control mechanism was impaired, with the result that an individual could perform any task well, but could not do it consistently (Stuss, 1987; Stuss *et al.*, 1989, 1994c – see also West & Alain, 2000a, 2000b, for the role of prefrontal cortex in maintaining optimal level of control in healthy young adults). We postulated that such a top-down control would involve the frontal lobes, but could not investigate this possibility with TBI patients because of the more diffuse nature of the disorder. To examine this hypothesis a study of IIV in patients with focal frontal and posterior brain damage was completed (Stuss *et al.*, 1999, 2003). The

results only partially confirmed the hypothesis. The frontal lobes were involved in a general top-down manner. However, it was not “frontal lobes” in a global sense. Three different regions were involved, each related to a different mechanism of control. Moreover, the posterior regions were also related to control, but only in one condition, which depended to a greater degree on a particular mode of cognitive processing – visual-spatial integration. The focal lesion study therefore suggested that there were different kinds of control of variability, some related to the specific content of the task (domain specific), perhaps more related to the posterior regions, and others more domain general, related to different regions within the frontal lobes.

The cerebellum has also been closely connected with IIV. If one accepts that temporal processing tasks are about variability, then the evidence is consistent that cerebellar damage affects temporal processing (Ivry & Keele, 1989; Ivry *et al.*, 1988). However, the type of task might again be relevant, with impairment on event-based timing tasks, but not on a continuously produced task (Spencer *et al.*, 2003).

### Neuropsychiatric disorders

Individuals with schizophrenia demonstrate greater IIV (Brown *et al.*, 2005; Schwartz *et al.*, 1989; Vinogradov *et al.*, 1998). It appears that IIV is independent of psychoticism, and primarily found in those with schizophrenia, and not in affective disorders (Schwartz *et al.*, 1989). There is an important situational factor which might be having a significant impact – medication (Meck, 1996).

Research in depression suggests that individual variability may occur not just in cognitive functions, but in personality variables (Monk *et al.*, 1991). Following the temporal characterization, variations can be seasonal (Reid *et al.*, 2000) or day-to-day (Nezlek *et al.*, 2001). The latter study showed that such variability can be specific; empathy varied daily in depressed individuals, and did not covary with other measures such as daily depressogenic thinking, and self-esteem.

## Potential mechanisms underlying variability

What is not known is whether the symptoms of variability should be rehabilitated, or whether it is essential to address the specific impaired mechanisms that cause variable performance. In this section, the postulated mechanisms underlying different types of variability are reviewed. Specific mechanisms underlying group variability are not discussed. Although the underlying cause of scatter can only be speculated in a global sense, the clinical importance of profile analysis recommends review. The emphasis will be on mechanisms of dispersion and inconsistency.

- Cognitive abilities within an individual are not equivalent in terms of performance levels. This “scatter” amongst different measures and abilities is often normal and not necessarily reflective of abnormalities.
- Intra-individual variability is most often interpreted as a disorder of top-down control. In cognitive psychology terminology, phrases such as attentional lapses are used. In neuropsychology, this control is related to the frontal lobes.
- There are different mechanisms of control within the frontal lobes: task setting (left lateral); monitoring and checking (right lateral); energisation (superior medial). Each results in IIV; the importance of uncovering the mechanism relates to the potential specificity of rehabilitation.
- Control mechanisms within the frontal lobes are domain general; that is, they apply to any cognitive function mediated by this region of the brain.
- There are also domain-specific functions, such that impairment of a particular posterior cognitive domain can result in increased IIV for that particular function.

### Scatter

Scatter of scores in an individual's profile has been a valuable measure for analyzing the relationships among test scores (Lezak, 1995). If there is a substantial difference between two test scores, the

implication has been made that the lower score reflects some abnormal condition. This, however, assumes that individuals have equivalent abilities across different cognitive domains.

In reality, however, individuals have very different abilities across different domains. Matarazzo and colleagues (Matarazzo & Herman, 1985; Matarazzo *et al.*, 1988; Matarazzo & Prifitera, 1989) examined the WAIS III and WAIS-R standardization sample. Over 85% of the sample had differences equaling or exceeding 5 scaled score points between highest and lowest scores; over 15% had differences over 9 scaled score points (3 SD). Schretlen and colleagues (2003) examined scatter over 32 measures derived from 15 neuropsychological tests. Not one individual in the sample of 197 healthy adults aged 20 to 92 years showed “consistent” performance across the different measures, when consistency was defined by a Maximum Discrepancy score (MD) of 1 SD or less. The MD ranged from 1.6 to 6.1. When the neuropsychological measures were compared with IQ estimated by the National Adult Reading Test, the average person's lowest score fell 1.9 MD below his/her IQ. Age affected the MD measure by only 5%; age-correcting the scores did not reduce the scatter. Importantly, the differences did not appear to be due to a small number of tests with unusual psychometric properties. Cognitive abilities within an individual are not equivalent.

### Dispersion and inconsistency

Intra-individual variability is commonly seen as a reflection of a disorder of control. In studies of normal populations, the prevailing theory is that IIV is related to attentional oscillations, attentional lapses or mental blocks (Bertelson & Joffe, 1963; Foley & Humphries, 1962; Obersteiner, 1879). This could be influenced by mental fatigue, since IIV is often related to task demand durations, and shown primarily (at least in older adults) in the tail end of the distribution (Hockey, 1983; Lorist *et al.*, 2002; Williams *et al.*, 2005). General slowing is not necessarily directly related to increased IIV (Stuss *et al.*, 2003). The notion that some type of attentional

control process is the major factor is supported by other data: distractors affect IIV (Jensen, 1992; Ulrich & Miller, 1994; Stuss *et al.*, 2003); older adults often reveal IIV under conditions of a more difficult task, interpreted as inefficiency of executive control processes (West *et al.*, 2002). The biological mechanism in normal adults is uncertain (see MacDonald *et al.*, 2006, for a review). Catecholamines have been shown to play a role in modulating signal to noise ratio of neurons. Thus, age-related variability may be related to catecholamine changes, with greater neural noise and consequently higher IIV (Li & Lindenberger, 1999).

Lesion data present the most compelling evidence that the frontal lobes, in particular specific areas within the frontal lobes, are significantly involved in mediating consistent behavior. Damage to the frontal lobes does result in increased IIV across a variety of tasks. This type of control is therefore considered to be domain general (Stuss, 2006), in that the processes are superordinate to any number of functional domains. The precise control mechanism depends on which brain region is damaged. That is, there are different control processes within the frontal regions, all of which might impact IIV (Stuss *et al.*, 2002): left lateral – task setting; right lateral – monitoring and checking; superior medial – energization (see also Macar *et al.*, 2002). Although the overt symptom may be increased IIV, the mechanisms resulting in increased IIV vary depending on lesion location (Stuss *et al.*, 2003). In rehabilitation, one probably needs to address the damaged mechanism, and not the symptom of increased IIV.

There are, in addition to the frontal lobe domain-general control processes, domain-specific control mechanisms. These are related to the brain regions involved with that specific cognitive function. As a consequence, likely under conditions of task complexity, damage to a particular non frontal region can result in increased IIV for that particular function. In a complex feature integration reaction time task (but not in simple single feature detection or simple RT), increased IIV was noted in posterior regions as well as frontal (damage to the frontal lobes increased IIV in many tasks) (Stuss *et al.*,

2003). In a similar manner, increased IIV has been reported in patients with right hemisphere lesions and neglect, and was a function of spatial position and not just a general increase in variability (Anderson *et al.*, 2000). Milberg and colleagues (2003) reported variability in lexical decision tasks after left brain injury.

### Clinical implications

This overview of variability has shown that there are different kinds of variability, and all may negatively influence rehabilitation efficacy. Although performance fluctuation is almost totally ignored in rehabilitation research, we outline some potential avenues of research and clinical application, and present representative case studies as examples. Analysis of performance variability adds new information above and beyond the general level of performance, and is different from “noise” (Lecerf *et al.*, 2004). Importantly, these individual differences are stable, and therefore amenable to investigation (Hultsch *et al.*, 2000; Rabbitt *et al.*, 2001; Stuss *et al.*, 2003). The impact may be at the level of knowledge, in that being aware of both group constitution and IIV may help in evaluating research on rehabilitation, and the efficacy of clinical interventions. There is a final possibility – perhaps the minimization of IIV should be the specific goal of rehabilitation.

- The clinician must be aware of the different types of variability.
- Scatter should not be over-interpreted for individual diagnostic purposes. At the same time, finding consistent patterns of scatter in specific populations can be very useful.
- There is some evidence that pharmacological or behavioral methods can minimize IIV. However, much research is required to investigate whether specific approaches need to be used for different control mechanisms.
- Intra-individual variability observed in malingering is likely dissociable from that found in neurological conditions.
- Not all variability is maladaptive.

### Group variability and scatter

Excessive variability between individuals within a group suggests that the group composition may not be appropriate. Even if significant *rehabilitation efficacy* is found there may be limitations to the generalizability of results.

Precipitous analysis of individual scatter of performance might lead to over-diagnosis. It would be inappropriate to make diagnostic inferences based only on scatter on psychometric variability (e.g., MD measurement) without clinical context, since in many cases rather large quantitative differences among abilities are normal (Schretlen *et al.*, 2003). The clinical context should consider many factors, including patient complaints, educational and work background (historical strengths and weaknesses), the situational context (e.g., depression), and test interactions. Knowledge of scatter can be used to establish hypotheses, which can be tested. For example, does the profile follow known syndromes, and does this make sense in light of the total history? At the same time, finding the consistency of profile across individuals can be used to great benefit, as in the example of what has been achieved in the learning disability field (e.g., Rourke, 1985).

### Assessment

Individual performance fluctuation is an important psychological phenomenon, which has to be considered in both assessment and treatment. Since IIV is virtually never examined clinically, it can be considered a “silent” disorder, which may be reasonably frequent considering all the potential factors affecting stability of performance. Being aware of, and assessing, IIV gives one insight into the processing capabilities of an individual. By varying conditions, insight might be obtained about the potential for learning capacity. In the elderly for example, retesting (practice) and comparing standard (speeded) vs. power (unspeeded) testing, showed that practice and power improved overall correct performance, although the power condition resulted in a different error pattern (Hofland *et al.*, 1981).

Another very significant implication of IIV is that one assessment of a patient may not be representative of their actual level of performance. What you see may not be what you get (Stuss, 1987). Assessing different measures of intra-subject variability provides knowledge that may be crucial to the patient’s ability to successfully return to work, and will help guide healthcare providers, caregivers and employers. Performing a task in a less stable manner than the majority of other individuals would have a direct impact on an employee’s evaluation.

#### Case study

The following case study illustrates two important points: intra-individual variability may be the most important index of impairment, against a background of apparently normal functioning; interpreting the IIV against the functional performance of the patient provided the clinical context for interpretation.

The patient was a young male who had been thrown out of a car as a result of an accident on a steep and winding road, hit a tree near the edge of a sharp ravine, and was not found for several days. The traumatic brain injury was considered severe based on biological markers, with a documented loss of consciousness of 2 days and an estimated post-traumatic amnesia of 6 weeks. The patient was seen as a litigant in a medical-legal case some 2 years post-injury. On examination, the patient had mild left facial droop and left-sided weakness. History was remarkable, in that there were few complaints. In fact, post-injury, the young man had done better in school than prior to the injury. He had developed a serious relationship and had returned to work. However, employment positions did not last very long, and the patient had no explanation for this employment failure. In most regards his neuropsychological examination was normal, particularly in light of the severity of his injury. There was no measurable or observed evidence of malingering. What was observed, however, was significant variability of performance. For example, after performing the WCST successfully according to at least one method of scoring (7 categories correct, during a full 128-card presentation), he began to lose set, and for an extended period of time was unable to perform the task correctly

(Stuss *et al.*, 2000b). Had the administration of the WCST been terminated at the end of six consecutive responses, the set loss would not have been demonstrated. He also exhibited IIV on our (at that time unpublished) RT paradigms (Stuss *et al.*, 1989, 2003). There was also inconsistency in performance from session to session. The one striking clinical finding, then, was abnormal IIV, but the awareness of that fact was uncommon in the 1980s. His parents were interviewed. They essentially denied all deficits, saying all that was needed was more effort on his part. In their opinion, the purpose of the neuropsychological examination was to find out where the effort was needed. They did wish that he would close his mouth (left side facial droop) when he ate, but that could be taught. Finally, the appropriate question was felicitously asked. The family owned a business that used machinery. When asked when the son would take over the business, they stated emphatically (paraphrased): “Are you crazy? We don’t know from one moment to the next what he might do.”

The son had done well post-injury because of the external formal structure of the family. As when the son was young, the parents had in essence again “become the frontal lobes” of their son, enabling him to use maximally whatever abilities he had. Their fears related to what they observed in the less controlled environment. The son’s IIV was also the reason he could not maintain consistent employment (see the title for Stuss *et al.*, 2003).

### Intra-individual variability and rehabilitation/treatment

Can IIV be treated? Time itself appears to be a healing factor, suggesting some brain plasticity. In a cross-sectional study of severe TBI comparing mean response times (RT) and IIV in patients 5 and 10 years post-injury, there was no change in mean RT (significantly slow), but IIV had notably diminished (Hetherington *et al.*, 1996). Wegesin & Stern (2004) found that estrogen use, but *not* estrogen plus progesterin, reduced age-related increase in IIV for at least one form of variability. Bleiberg and colleagues (1993) administered dextroamphetamine in a single subject placebo crossover design to an individual with TBI. With pharmacological treatment

only, variability decreased. However, since only the standard deviation was reported, it is uncertain what the relationship to RT speed was.

There is some suggestion that behavioral interventions may have a beneficial effect. Intra-individual variability can be reduced with practice (Ram *et al.*, 2005), although it may be that there are both adaptive (practice) and maladaptive IIV in the same individuals over time (Allaire & Marsiske, 2005). It is likely that practice alone is not the best intervention.

What may be required is practice combined with cognitive rehabilitation of the specific impaired mechanism. Different control mechanisms within the frontal lobes have been postulated (Stuss *et al.*, 2003). Rather than generic rehabilitation to assist individuals with specific disturbances, knowledge of the lesion location and isolation of the specific deficits through appropriate assessment may provide at least a base for rehabilitation research efforts in rehabilitation targeted at the deficit.

#### Case study

This case illustrates the potential value of Luria’s verbal self-regulation in minimizing IIV, at least in a patient with focal right hemisphere pathology.

A middle-aged gentleman was seen in investigation prior to surgical removal of a large hypodense lesion in the right frontal lobe with extension to the right parietal region (Stuss *et al.*, 1987). The most striking disorder exhibited was motor impersistence, a disorder most commonly found after right frontal pathology when damage is focal. He could initiate tasks successfully (e.g., close your eyes, hold your breath), but could not sustain them. He was also variable in other simple tasks, such as continuous tapping. We used verbal self-regulation (Luria, 1973; Meichenbaum, 1974) to reduce the motor impersistence. If a specific command was repeated within a relatively brief period of time, the patient could sustain the task as long as the command was repeated. The patient then was able to internalize this procedure and repeated the command himself. In anatomical terms, it is likely that his intact left frontal task-setting mechanism could assist the impaired right frontal monitoring and checking mechanism

to sustain behavior. However, this patient's use of self-regulation was fragile, in that it was easily disrupted by distractions.

With certain patients, it may be necessary to externalize the control of the patient (see case study above) (Stuss, 1987; Stuss *et al.*, 1994b); i.e., establish a sufficiently rigid external environment that acts to minimize the necessity of top-down control, allowing responses to be more automatic. In such instances, the employer or care-provider has to be a partner, and indeed the leader, in rehabilitation.

#### Case study

A young man who had suffered a severe TBI returned to work as an autobody mechanic. His performance at work was normal in most aspects. However, if unable to complete a specific task adequately, he would become volatile and destroy what had already been successfully accomplished. His employer, who had suffered a severe TBI himself and had been our patient, over time had learned that external control would help him with his problems. He became aware of the signs preceding such eruptions in his employee, and intervened by telling the young man to take a 5-minute break. The young man would then come back and finish the job without any difficulty. The employer recognized the cause of the variable and erratic performance, and provided external prosthetic time outs to help stabilize performance.

### Intra-individual variability and malingering

How might the concept of intra-individual variability relate to the observation of inconsistent performance in malingerers? That is, might variability be a reflection of trying less hard? Cullum *et al.* (1991) proposed that it would be difficult to have the same levels of poor effort over multiple tests; that is, it is difficult to fake consistently. Reitan & Wolfson (1997) compared two traumatic brain-injured groups, one in litigation and the other not, in a 1-year test-retest, and reported that the group in litigation had less consistent scores. Strauss and colleagues (2000) repeated testing on three

occasions with undergraduate students who were asked to pretend to have real impairment to win a lawsuit (malingerers) or do their best. The “malingerer” group had less consistent mean scores across the test sessions. What then is the difference between the dispersion and inconsistency caused by brain damage or malingering?

A possible answer can be found in the nature and extent of intra-individual variability as expressed in patients. The principle of “making sense” (Stuss, 1995) can be invoked here. That is, IIV as noted does follow certain principles. It is primarily expected in more complex tasks. IIV is itself consistent. Moreover, in many instances the mean performance of our focal lesion groups was not abnormal, in contrast to many malingerers who present as very significantly impaired. Just as caution is required in interpreting scatter, dispersion and inconsistency must be considered clinically as information that must be interpreted scientifically – by establishing hypotheses and further testing.

### General conclusions

The tone of this chapter might suggest that IIV is maladaptive. In fact, our position is that variability of performance is a normal, constant presence in all individuals, and can be either maladaptive or adaptive. The nature of control processes is not just to make processes automatic and uniform, unless this is for the benefit of the organism. Control at some level also requires flexibility in examining options of behavioral responses, and such flexibility will of necessity lead to variability in behavior. Moreover, there are likely levels of control and variability, and the interaction of these need to be studied in greater detail (see Stuss *et al.*, 2001b, for a discussion of levels of control in self-awareness). The brain is a highly distributed super-system, with control at different processing levels (Adi-Japha & Freeman, 2000). This is very aptly illustrated in a study by Miller and colleagues (1996). Patients with Parkinson's disease were treated for gait disturbances. As gait improved, with reduced variability,

there was increased variability in muscle and brain measurements. The ultimate goal is to understand and harness both adaptive and maladaptive variability, not to create automatic robotic behaviors.

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