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Individual differences in cognitive neuropsychology

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ABSTRACT

Professor Bob Stelmack from the University of Ottawa (I was a graduate student at U of O when he started his career there) stressed both as a teacher and a researcher the importance of individual differences. In neuropsychology, this is often evidenced by the problems of variability of performance within a supposedly well-defined homogeneous group. This review presents examples from my research in traumatic brain injury and the effects of frontal lobe focal pathology to illustrate how an emphasis on individual differences had to be applied to advance the understanding of specific brain-behaviour relations and the role of the frontal lobes in human behaviour. This focus is equally relevant in organizing a larger scale research structure integrating diverse sources of information (e.g., genetic to behavioural) and basic and clinical science to improve diagnoses and treatment – the push to more individualized care.

1. Introduction

Many years ago, I was a graduate student in the School of Psychology at the University of Ottawa. I was a high school teacher, who was taking clinical psychology to gain knowledge and skill sets in counselling students. Although the psychology program was primarily clinical, there was an experimental arm, and the clinical students were also required to take the experimental courses, which included lab research.

The professors in the program were excellent, and we learned truly fundamental principles in psychological research and analyses. One of these was a young (as a mature student, I even may have been older) assistant professor, Bob Stelmack. I remember Bob's labs in particular, not only because of his enthusiasm and emphasis on quality but also because he used unique (to my naïve mind) techniques such as pupilometers. In these labs, and in his courses, in addition to strict experimental design, Professor Stelmack often stressed the importance of individual differences.

Instead of returning to teach high school, I continued in the clinical, then academic, path of psychology, specializing in brain-behaviour relations and neuropsychology. Because of the focus of my research, my collaborators were often neurologists, psychiatrists, and imagers. The individuals studied were not undergraduate students, but those with a specific disorder or disease. As will be seen, the emphasis on individual differences must have been ingrained deeply.

2. Individual differences and variance

The study of individual differences has its flipside in the understanding of variance, both at the group and individual level, and indeed even at level of research organization. Examples will be given about the evolution of my own work in science and research administration that was dependent on the lens of individual differences. Examples in this paper will be of group variability. The emphasis is on the group variability; details of the actual research can be gleaned from the original publications.

2.1. Examples from studies in traumatic brain injury

Clinical research is often designed based on a question related to the diagnosis and/or treatment of patients. The individuals being studied are usually designated by current clinical standards. Relatively early in my career, the importance of group inclusion came to the fore. The objective of a particular clinical study was related to patients who had suffered a traumatic brain injury (TBI) and were by then current diagnostic criteria, including the standard neuropsychological tests, considered to have achieved good recovery (Stuss et al., 1985). It was the patients, however, who said they were experiencing significant continuing problems.

The question then – were we missing a significant problem undetectable with our standard assessment procedures? A literature review of growing evidence on the pathophysiology of TBI suggested notable involvement of the frontal lobes and frontal systems in virtually all TBI cases. There is often a classic dissociation in individuals with frontal lobe pathology – they can perform automatic over-learned tasks well including standard intelligence tests, but may have difficulty in less

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routine situations. On review, the neuropsychological measures we were using were not as sensitive to the effects of frontal lobe damage.

The patients were identifying these problems in their daily lives which had multiple and often conflicting or concurrent demands. We modified our assessment procedures, and published the results - these "subtle" effects of TBI were indeed real and made sense with the known pathophysiology. However, a closer look at the data (Stuss, 1987) indicated that, despite the highly significant differentiation between the TBI and matched control groups ($p = 0.002$), the strength of individual correct classification varied, and three controls were identified as TBI and 3 TBI as being normal. The data we had gathered on all individuals did not allow us to identify the reasons for the group variability, but it did start to open our eyes for a greater focus on individual differences.

There was a somewhat more successful endeavour in a TBI project studying the operational definition of post-traumatic amnesia (PTA), and its course of recovery related to severity of TBI. We assessed five groups of individuals: three groups of individuals hospitalized because of a TBI, divided by the Glasgow Coma Scale into three levels of severity of injury – mild, moderate and severe; two matched control groups – one a hospitalized orthopaedic surgery control, and the other a non-hospitalized neurologically normal group. All were tested daily on a series of rather simple bedside attentional and memory tasks, until they reached criterion. For the measure of PTA, we used the classic Galveston Orientation and Amnesia Test (GOAT), and the recall of three words over a 24 h delay, a test more in harmony with some earlier measures of PTA.

The first important result finding was that, in at least the mild and probably the moderate TBI groups, the "amnesia" was attributable to a post-traumatic confusional state affecting encoding of information, rather than a hippocampal amnesia (Stuss et al., 1999). Second, the three little word test was more sensitive to ongoing problems in recovery than the GOAT (Schwartz et al., 1998). Third, the TBI patients recovered more slowly than both control groups and the course of recovery followed the level of severity in broad strokes but there were subgroups *within* each category of severity, and overlap *between* levels of TBI severity (Stuss et al., 1999). That is, the classic definition of TBI severity was inadequately sensitive to classify subgroups of individuals in relation to the important psychological ability to have daily memory.

We looked for the factors that would improve subgroup classification (Stuss et al., 2000) using a statistical regression technique that separates by extremes of performance (Classification and Regression Tree; Breiman, Friedman, Olshen, & Stone, 1984). The dependent measure was the time to achieve a perfect free recall score on the 3 words recall over 24 h. The results indicated at least 8 subgroups as defined by recovery from PTA, the recovery related to different factors such as the Glasgow Coma Scale, age, duration of loss of consciousness, and relation to location of soft tissue injury. Unfortunately at that time of research we did not have genetic measures or sophisticated imaging procedures that might have provided even greater specificity.

The emphasis on individual differences and improved phenotyping did yield multiple practical results. Physicians and health care givers would have better knowledge to inform families and patients on the likely course of recovery events. Expectations for these families and patients would be more realistic. And at the research level, the results provided an opportunity to investigate particular mechanisms related to trauma and recovery, with possibly more specific treatment.

2.2. Examples from studies in individual with focal frontal lobe lesions

The importance of more refined group phenotyping was perhaps most evident on our work on understanding the functions of the frontal lobes. Many of the theories posited a more central unifying role of the frontal lobes. Knowledge of anatomical development, architectonic specificity, and neuronal systems as well as animal research suggested a contrary view – the functions of the frontal lobes may have a more precise anatomy/function relationship.

Four of us (Tim Shallice, Mick Alexander, myself and Terry Picton, the latter also formerly cross-appointed to U of O Psychology) shared our knowledge and approaches to create a theoretical and experimental approach to study the functions of the frontal lobes. Our initial efforts were not fruitful, despite a strong theoretical base and precision in patient inclusion. Eventually we realized that the problem was group phenotyping. We were using traditional anatomical groupings, and the variance was large.

Over time we evolved different ways to sub-classify the frontal patients into new anatomical groupings (Stuss, 2016). These included lesion overlap, behavioural outcomes, statistical comparison to control groups, the CART, and eventually efforts to achieve architectonic specific brain-behaviour correlates. These data are presented in a series of papers, and perhaps best summarized in the following: Stuss & Alexander, 2007; Shallice & Gillingham 2013. The attentional research, in conjunction with other studies behavioural/emotional self-regulation and theory of mind/metacognition, led to a more complete model of frontal lobe functions, compatible with anatomy and connectivity (Stuss, 2011a).

The value of striving for individual differences, at least finer group sub-stratification, is theoretically relevant. It is also of importance clinically. I combined the efforts in TBI with those of focal frontal lobe injuries. The knowledge of frontal functional localization can be used to understand at least some of the subtypes of individuals with TBI (Stuss, 2011b).

2.3. Organizing research to strive for personalize medicine

The emphasis today on personalized medicine (terms also used are precision medicine, stratified medicine, although not totally interchangeable) is in reality a reflection of the importance of individual differences. The goal is to understand the multiple factors related to the development and course of disease by using informatics approaches to develop new categories and diagnoses that will tailor the intervention for a specific person, or persons within a more defined subtype.

The government of the Province of Ontario had decided to maximize the impact of the clinical and research strength in Ontario to address the important brain disorders. As founding President and Scientific Director of the Ontario Brain Institute [OBI] (Stuss, 2014, 2015), there was an opportunity to apply the lessons learned in group subtyping to patients with neurological and mental health diseases to advance science and through science clinical impact. Researchers and clinicians across the Province of Ontario were integrated into what we called "Integrated Discovery Programs".

Integrated described many levels of working together: across institutions, across disciplines (neurology, psychiatry, psychology…), with many modalities of measurements (i.e., genetic, behavioural, imaging, etc.), and involving not only clinicians and basic researchers, but also patients, caregivers and family advocacy groups. The process of integration required standardized research based assessments no matter where the patient was seen in the province, and the gathering of data into a secure informatics platform that would allow robust statistical analyses (big data) and sharing of data. *Discovery* not only meant hypothesis driven research, but an openness to the potential of a data driven approach, particularly in relation to the finding of more refined diagnostic categories and the study of mechanisms of disease within and across current diagnostic categories. The term *Programs* identified an approach that included but went far beyond a series of research projects.

The programs were also established to maximize clinical impact. Research has to be translated into products that are provided for patients. Companies were integrated into research discussions, not to drive science, but to be present to link product development at an earlier stage of discovery. There was also an integration of the beneficiaries (patients,