Single Case Studies as Seeds:
Brain Models That Matter

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ABSTRACT

Single case studies are research studies of single participants. They explore new ideas and can suggest extensions in methods and for treatment (Yin, 1984). In this article the case study refers only to conditions observed and is limited to what was observed from these comparisons between normal function and patterns of specific conditions. This does not reflect the theory of a formal case study but rather it is an attempt to show the case study and simple computer modelling as learning tools in a complex environment. Critics of case study methodology cite small case numbers as not having grounds for establishing reliability or generalization of findings and that the intensity of exposure needed for thorough case studies could bias the research findings subtracting from researcher objectivity. Early computer models were used to simulate the function of the brain and provide partial answers. They provided insight into the understanding of complex function. In recent history, computer models and case studies have been cast aside in favor of live brain imaging and complex biochemical reactions. It is good to remember that these tools brought us to the place of knowledge we enjoy today and have enlarged diagnostic and treatment choices. They are still valuable and inexpensive methods that can impact the imaginations of neuroscientists and kindle their passions to solve the complexities of the human mind one problem at a time. Greater rigor can be easily maintained by adopting a format whereby a patient would be assessed by a fully standardized neuropsychological battery and the performance then compared to large sample of normative data. The formal study is important for generalization of findings across conditions and can be applied once normative data has been collected as a basis for comparison.

Keywords: *Brain Training, Case Series, Case Studies, Cognitive Rehabilitation, Connectionist Modeling, Dyslexia, Neurogenesis, Neuroplasticity, Picks Disease, Self Regulation, Stroke, Traumatic Brain Injury*

BACKGROUND OF CASE STUDY EXPOSURE

Single case studies and connectionist modelling can give uncommon insight into human behaviour and rehabilitation after neurological insult. In this article a strong focus is given to the art of reading as it serves as a pivotal focus for observing dysfunction and rehabilitative potential Naish (2000) states "Reading employs symbols of symbols and the processing required to link the written word with the original concept has been considered by some to be so complex that if we could understand fully how it took place we would effectively understand the whole of human cognition" Excerpts by Cohen, Johnston and Plunkett (2000) and Parkin (1996) refer to reading and cognition issues associated with the use of single studies to generate theories and relate they have had immense exploratory value.

A single case study may reveal patterns that generate an insight. When this pattern is compared to similar conditions research strategies can emerge. As single case studies

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are combined with similar case studies, double disassociations, cognitive modelling and neuron imaging the resulting data sets can produce a robust model. The increase of computer based communication makes it possible for scientists to collaborate internationally on single case studies, evolving case series or computer based data that represents models of human behaviour during neurodegenerative insult.

Greenhalgh (1997) refers to single case studies as the quick and dirty method for extracting research information and lists their inclusion at the bottom of the research hierarchy in regards to evidence. She later qualifies this statement, stating that when single case studies are well done they can yield superior detail generally lost in larger studies (Greenhalgh, 1997).

Single case studies are crucial when an observation requires rapid attention even though methodological links are weak. For example three children at school go out to play before reading class and one child dares the other two to eat 'mushrooms' on the playground, they are poisonous but taste fine and the two children continue to play but later show a loss of balance, hallucinations and inability to read in class. Knowledge based on a single case study on mushroom poisoning could result in recognizing the progression of circumstances and taking appropriate action to save the children's lives. Large randomized double blind studies could determine correlation factors and average rate of poison over time; however the available single case study information is appropriate for immediate intervention.

Rather than focusing solely on the value of single case studies or that of connectionist models they will be seen as seeds of research. How this seed is tended determines its core qualities and its capacity to reproduce in the field of research. It is good to bear in mind that without an initial 'seed' the likelihood of a major double blind clinical trial is slim. Likewise, undue emphasis on finding disassociations and grouping deficits into convenient "syndromes" can mask individual differences and invoke dichotomies.

The value of single case studies hinge on circumstances surrounding reports, the skill with which they are presented and ways they are integrated with other research. Using dysfunctional models to illuminate normal function is risky in that the dysfunctional component can influence the working areas surrounding it and so confound the model (Cohen, 2000). Case studies may be thought to lack credibility as they are not sufficient to determine the development of generalizable results. Although this work uses the case studies as a teaching tool there are more rigorous forms of single case study methods developed within this field that have greatly added to the scientific method and contain the potential for validating the areas of interest for more detailed scientific exploration (Crawford, 2011) There is an excellent resource for adopting case studies into clinical practice at http://homepages.abdn.ac.uk/j.crawford/pages/dept/SingleCaseMethodology.htm.

EXEMPLAR BRAIN CASE STUDIES

Clive Wearing

In memory research archives we find Clive Wearing who was the basis of a well-known single case study. Everyday is literally a new day for him because he remembers nothing consciously from the day before and yet he is still able to preserve some function. His amnesia, memory deficits and history as a former orchestra conductor are presented at conferences, displayed on you tube and written up as segments in the memory research of famed scientists. Wearing apparently maintains reading ability and plays the piano, however available research fails to address how well he reads to comprehend or conceptualize new materials (Posner & Rothbart, 2007; Wearing, 2005). Individuals other than Wearing sustain similar assaults from conditions such as herpes encephalitis (Patel, 2009) but Clive was popular in UK society when scientists were exploring the frontiers of working memory and his plight captured the imagination of the public (Wearing, 2005).

Phineas Gage

Phineas Gage is an example of a single case study, who sustained walking, talking and even his reading competency reading after an explosion drove a tamping iron through one side of his skull. Regrettably his personality sustained irrevocable changes (Phineas Gage Foundation, 2010). His injury kindled evidence for exploring brain localization whilst his partial recovery sparked hope for neuroplasticity. Memory embedded for reading could have been utilized for building compensatory strategies for other areas of his life (Ball, 2002).There are single case studies where recognition and naming remain relatively intact while writing is impaired when tested in other ways. Patients were able to write and name even when other routes failed (Ellis & Young, 1988). Case studies combined with experiments in cognitive modelling allow brain scientists to test learning patterns and identify ways function could be preserved based on the learning patterns of original case studies,

Gladiators sustained similar traumatic brain injury fates centuries ago and lived and died without comment save from the occasional philosopher, although lately with new forensic techniques examination is possible (Kanz & Grosschmidt, 2006). It appears single case studies are moderated by social interest as well as scientific research that may influence funding favor.

Dr. Arnold Pick identified Pick's disease in 1892 using the single case study of a man who presented with dementia and progressive speech loss, after death his brain autopsy displayed signs of atrophy. He later joined this example with a case series and multiple autopsies of similarly afflicted individuals tested by observation and psychometrics. Magnetic resonance imaging (MRI) and other sophisticated equipment were not yet available (Todman, 2009).

Comparing Pick's Disease with Brain Trauma

An anonymous case study of a former solicitor with Pick's disease reports he experienced emotional dysfunction and reduced social consciousness. This is consistent with reports of Phineas Gage's behaviour after he sustained left temporal lobe damage/pre-frontal cortex injury through a traumatic brain injury. In this case damage would be immediate from trauma, and be multiplied by secondary axonal damage days to months later resulting in a gradual loss of cognitive function due to his inability to communicate appropriately in order to maintain sensory stimulation (Carlson, 2007).

These single case studies both point to left temporal lobes as well as pre-frontal cortex involvement as being important for cognitive control, social awareness and self-regulation. Even with similar areas of dysfunction the intervention is different. Pick's disease is neurodegenerative and progressive so permanent rehabilitation is not probable but will contribute to the patient's quality of life. A traumatic brain injury or stroke patient is likely to maintain cognitive gains made in rehabilitation.

Sachdev (2009) states former employment and significant social skills may provide initial neuron-protection, however these assets are not sufficient to aid recovery with advanced dysfunction. Initial theory regarding neuronal protection and plasticity was tested using simple computer connectionist learning models. Even the most advanced connectionist models are not sufficient for complexity to produce multiple parallel processes and the resulting effects that can be seen by observing a living human. They are useful though because they can repeat simple patterns under multiple conditions and can be tested repeatedly without frustration unlike dealing with fragile human persons. Connectionist models can show us commonly developed patterns by inputting extensive information versus less information and then simulate the effects of brain lesions by electrically altering or lesioning thesemodels. Connectionist modelling can explore recovery models but even with this simple tool the first step comes with observation of a single human person who becomes like a seed for ideas and research (Naish, 2000).

For an example of case studies and connectionist modelling working together we can look at a case of Pick's disease in a local solicitor and the difference between this condition and that of traumatic brain injury. The solicitor's degeneration from Pick's Disease was neuron-degenerative and progressive as confirmed by biopsy and indicative of overall present IQ of 85. Pick's disease patients such as the solicitor may retain spatial ability and memory. Pick's disease can present with language disorders as evidenced by the solicitor pronouncing a fork tine as a 'stig'. At life's end Pick's disease patients would show craters and scarring where that area of brain should have been whereas trauma could show shrinkage or atrophy in damaged areas. Pick's Disease unlike trauma has an easily identified genetic component. Inherited forms of Pick's disease are linked to abnormalities on chromosomes 3 and 17 (NINDS, 2010). Reading may increase quality of life for the solicitor or anyone with early Pick's disease and may moderate the progressive failure of object recognition and social skills.

Testing could be done with the solicitor for various forms of acquired dyslexia to develop functional adaptation strategies such as accessing alternate reading routes. A speech pathologist could enable him to minimise language issues entailed with the phonological processing deficits incurred with this neurodegenerative disease progression. The damage appears bilateral and extensive but given his professional background it would be prudent to see if cognitive reserve could slow down the course of the disability as advised by the research of (Valenzuela, Sachdev, Wen, Chen, & Brodaty, 2008) despite potentially conflicting reports links between cognitive reserve, failure and function are unclear possibly because individual function and recovery in neurodegenerative conditions is difficult to generalize statistically.

Help for Quality of Life and Functional Capacity

Both the solicitor and a brain injury patient may benefit from a trial of bio-feedback, variable heart rate training and facial expression/body language training to assist him in finding compensatory strategies with which to recognize social cues (Williams, Brown, Kemp et al., 2006; NINDS, 2010). In Pick's disease supervised (due to dementia) consistent physical activity as evidenced by (MRI) may increase neuroplasticity at the white/grey matter interfaces in the brain and so delay results of degeneration (Greenwood, 2007). In a traumatic injury case the gains in white matter would also be realized but they are more likely to happen faster and be maintained throughout the life of the patient.

Reading appears to be a robust process with neurogenesis contributing to adaptation due to injury. This process can be seen in case series of brain injured children where multiple areas of the brain are damaged but reading ability is spared, albeit not always with comparable fluency. Single case studies demonstrate reading fluency retention partially dependent on how completely reading was ingrained pre-injury. This factor was robust and consistent with neuroplasticity factors common to growing children (Ewing-Cobbs, & Barnes, 2002).

Patterson and Bessner cited in Parkin (1996) argued individuals can adapt to reading from either hemisphere by testing single case studies of split brain patients and contrasting these with deep dyslexia patients who are thought to read with the right brain, their premise was should reading be exclusively hemisphere dominant, split brain and deep dyslexic patients would do equally well, when in fact the deep dyslexia patients scored much higher.

Logging Adaptations Through Cognitive Models

Attempts to test normal individuals were interesting as they showed adaptive patterns in the brain. Stimuli were applied to left visual fields below the level of conscious perception (<200 ms) as above this participants consciously switched visual fields (Parkin, 1993). < 200ms reveals perception and bottom up processing rather than the top down effort conscious reading requires as established by Naish (2000). Connectionist models used by Hinton and Shallice (1991), and Plaut and Shallice (1993A&B) developed lesioning patterns to mimic deep dyslexia in normal reading models and were able to produce them in semantic memory models similar to those sustained by deep dyslexia. Plaut, and Shallice (1993b), suggest investigation of the duplications of disassociation without specifying modular boundaries between concrete images and abstract but subject related words.

Cognitive Models can be supportive in logging where, and to what extent cognitive functioning is systematically impaired or spared. They can offer insight as to whether the function in question is mainly modular or if it is distributed like a network as in the case of executive function and reasoning (Cohen, 2000; McLeod, Plunkett, & Rolls, 1998; Parkin, 1993). Damaged brains are highly individual but with common factors, inclusive of cultural and emotional aspects whereas computer models are systematic, can be lesioned and outcomes tested mathematically and repeatedly. Associations or double disassociations can be produced and observed in connectionist models without ethical consequences. Models are cost effective, adjustable, need no recruitment or institutional review board approval, if the experiment damages them no ethical harm is done. Models fail to reach the complexity of human cognitive networks and it is difficult to determine if what the model learns is pertinent or how it will perform across the range of individual differences.

Hinton and Shallice's (1991) network was described as a single route reading model. The error was summed across hidden layers, which would make this not a singular route but rather a modular component with network qualities. Models can be useful tools when described correctly and partnered with relevant corroborating neuropsychological or imaging evidence but are of themselves not stand-alone products (Posner & Rothbart, 2007).

Complex reading and writing behaviours and skills interact with the level of functioning of other cognitive systems and this provides a challenge in determining if a deficit is modular specific. Chialant and Caramazza (1998) suggest reading impairment could result from degraded transfers between language and visual processes. Processing speed, light sensitivity, attentional deficits, visual and auditory working memory, saccadic eye movement, visual neglect, language impairments, sustained comprehension with increased cognitive load, extraneous sensory filtering capacity, individual differences and even chronic pain levels could influence reading and writing behaviours (Carlson, 2007).

Brain Injury is Specific and Rehabilitation Needs to be Targeted to be Effective

We now turn to the single case study of an anonymous university student who collapsed with a stroke at a summer school disco. The data we received on which we hoped to base her treatment was incomplete. This is quite common in clinical settings where clinicians deal with partial information and incomplete histories. It would be helpful to have access to pre-existing conditions other than only the hypertension she was said to have suffered and her raw post injury psychometric scores.

The initial brain scan showed a large hemorrhage in the left tempero-parietal region, whereas a recent MRI scan describes this to be resolved. The transient visual field neglect the student sustains may not be adequately resolved to address complex learning involving executive function network Hospital grade MRI's may lack the clarity for definitive finer brain diagnostics found in research grade equipment. The pattern of her errors may be significant for unilateral neglect if errors are left side dominant on the page or if writing consistently ignores the left margin and starts closer to the page's centre.

There was MRI evidence of an infarction in the posterior temporal region. Sustained hypertension can also result in kidney impairment and heart damage. These are factors in toxicity and cerebral hypoxia respectively and could influence cognition. Prescribed medications or headaches may influence vision and reading performance. Further investigation to determine the extent of secondary axonal death, damage to central nervous system networks and how these factors inform her present cognition would be advised.

With a verbal and reading IQ of 119 even post stroke, it is presumed she retained reading ability however this measure does not differentiate between her ability to integrate old materials with learning of novel concepts. Useful information to facilitate cognitive recovery could be recovered bytesting for photosensitivity, words distorted or seeming to move on pages, spelling skill retention, transposition between two and three dimensional objects, working memory retrieval with cognitive loading, conceptual understanding and processing speed for new learning through visual and auditory channels.

She presents with a difficulty in sounding words out. This is phonological rather than rule based, as she was able to sound out quite complex words but had difficulty with regularizations, which would be consistent with a left parietal temporal infarct (Parkin, 1996).

Her sensory filtering capacity may be compromised could impact comprehension when tired, or with competing events in her environment (Persson & Reuter-Lorenz, 2008). This may indicate pre frontal and/or somato-sensory cortex deficits or that the stroke degraded auditory and visual processing speed (Carlson, 2007). Memory recovery strengths indicate that as she writes or draws she could uncover resources available for compensatory strategies. All these factors and more need weighing to deliver a diagnosis capable of informing individual treatment and would be important to define to reduce confounding variables if single case studies are intended to support a research model.

Tools for the Journey Can Start With the Case Study

Single case studies and computer connectionist modelling are not the full array of tools for brain science research but they are like valuable kindling, which starts a fire and is insignificant when working alone but capable of provoking warmth for many when appropriately applied.

Often it is the writing savvy of a scientist and author like Oliver Sacks who can highlight the salient points of a case study and bring it to life. He shared how music rewrote the paths in his brain and allowed him to make it to safety despite proprioception damage (Sacks, 2007). His innovative way of recording his experience as a case study provided foundational inroads where after others read of his experience they were inspired to apply this experience in a formative research question for Parkinson's Disease. It was found that Parkinson's patients who could barely walk could learn to move effortlessly with music (Artignoni, Acchetti, Ancini, Glieri, & Appi et al., 2000).

Single Case Studies Reveal the Experience of the Struggles Within

Dr Sack later introduces us to a man who mistakes his wife for a hat, an event with profound implications for cognition and identity. Another of Sack's single case studies highlights 'The Mariner' a victim of Korsakoff's psychosis, (amnesic-confabulatory syndrome) and describes life through a man fixated in the present. Through the journey of the case study we are taught what it is like to live with a mind that does not mirror reality. Readers are asked to consider the state of his soul being unable to envision his past to repent for it or his future to indicate future intent.

Sacks, (1985) causes readers to reflect on how experience past and future impacts choice and informs consciousness. It may be asked, what would prompt science to care? Scientists are individuals moved by the same passions and feelings we all share, when they care, they think and imagine when they think, solutions are born. The seed of a case study born of observation and imagination can produce a harvest of data as can a harvest of valuable patterns discerned through connectionist models.

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