Clinical and experimental neuropsychology

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Neuropsychology is a form of neuroscience interested in investigating and uncovering the nature of the relationship between the mind and brain (Beaumont, 2008). Clinical neuropsychology is concerned with diagnosing, treating and rehabilitating patients with brain pathology, whilst experimental neuropsychology is concerned with discovering normal models of cognition and understanding the brain functions of healthy individuals (Ogden, 1996). However, clinical and experimental neuropsychology, whilst separate disciplines, are not mutually exclusive as clinical patients are used to help formulate normal models of cognition and brain function in experimental neuropsychology, whilst clinical neuropsychology uses normal models of cognition to help treat and rehabilitate clinical patients (Marshall & Gurd, 2003). The current essay examines this interdependent relationship, focusing exclusively within the domain of explicit and implicit long-term memory (LTM).

Atkinson and Shiffrin (1968), in their multi-store model of memory, proposed a single LTM store for holding large amounts of information over long periods of time. However, it is now recognised that the variety of information that needs to be stored in LTM means that it is not easily conceptualised as a unitary store (Eysenck & Keane, 2005). LTM has since been conceptualised as consisting of two major systems: explicit and implicit memory (Graf & Schacter, 1985; Schacter & Tulving, 1994). Implicit memory reflects the unconscious, unintentional, and indirect retrieval of information, whilst explicit memory reflects conscious, intentional and direct retrieval (Schacter, 1987; Hudson, Flowers & Roberts, 2009). Implicit memory can be measured through tasks assessing priming, such as word-stem completion, in which

participants are asked to complete stems, such as “ cra_ _”, to form the first word that comes to mind (Jacoby, Toth & Yonelinas, 1993; Roediger, Weldon, Stadler, & Riegler, 1992). The increased use of previously presented words, which participants are not told to remember, is indicative of these words being present in implicit memory (Mulligan & Hartman, 1996). Explicit memory is investigated through tests of recall and recognition (see Schacter, 1987) where participants are told to try to remember the study words to be used in a later memory test. It has, however, been noted that with neurotypical individuals, where implicit and explicit memory function as normal, explicit processes may unintentionally contaminate measures of implicit memory (Butler & Berry, 2001). Jacoby (1991), therefore, proposed the process-dissociation procedure (PDP), an oppositional method that measures both implicit and explicit memory processes within the same task to derive uncontaminated estimates of these memory processes. Despite some criticisms of this method, such as the complexity of the instructions (Graf & Komatsu, 1994), studies using the PDP have reliably suggested that implicit and explicit memory are functionally dissociable in neurotypical individuals (Hudson, 2008; Jennings & Jacoby, 1993; Mulligan, 1998; Titov & Knight, 1997; Toth, Reingold & Jacoby, 1994). However, clinical neuropsychological patients have been fundamental in supporting this dissociation and in uncovering the neural areas underlying implicit and explicit memory.

One of the most extensively studied neuropsychological patients, H. M., was instrumental in supporting the division of LTM into explicit and implicit memory, as well as in elucidating the neural areas underlying explicit

memory. H. M. underwent bilateral MTL resection to treat severe epilepsy (see Scoville & Milner, 2000). Post-surgical psychological profiling revealed H. M. to have no deficits in intelligence, perception, abstract thinking, or reasoning abilities. However, H. M.’s score on the Wechsler Memory Scale (WMS; Wechsler, 1945) revealed that H. M. had severely impaired explicit memory abilities, in that he could not learn new explicit memories (Scoville & Milner, 2000). Experimental investigations of H. M. confirmed that he had impaired explicit memory functioning (Gabrieli, Cohen & Corkin, 1988), but that H. M. had intact priming abilities, as evidenced by faster reaction times in response to previously presented real and pseudo-words (Keane, Gabrieli, Mapstone, Johnson & Corkin, 1995). Therefore evidence has shown that H. M. had an intact implicit memory system in the absence of explicit memory. Additionally, the fact that H. M. had profound explicit memory impairment suggested that intact MTLs were necessary for the normal functioning of explicit memory. The importance of the MTLs for explicit memory has been further strengthened by studies utilising the PDP to investigate patients with temporal lobe epilepsy (TLE). Del Vecchio, Liporace, Nei, Sperling and Tracy (2004) and Hudson et al. (2009) used the PDP, and found that patients with TLE showed impaired explicit memory abilities, but intact implicit memory abilities. Additionally, Hudson et al. (2009) found that explicit memory deficits were only present in patients with left TLE, suggesting that explicit memory abilities may be localisable to the left hemisphere. The hemispheric localisation of explicit memory has become an important principle in one method for treating epilepsy; the Wada test. The Wada test is a clinical neuropsychological procedure that mimics the surgical effects of temporal lobe resection on language and memory (Lehéricy et al., 2000). The Wada

test provides a useful example of how experimental neuropsychology has influenced clinical neuropsychology, as the Wada procedure was developed out of experimental neuropsychological findings that memory and language are structurally dissociable (e. g. H. M. who had explicit memory deficits but intact language abilities after undergoing bilateral MTL resection). However, as the Wada test was developed out of studies of hemispheric language dominance, it will not be discussed in further detail here.

Another clinical patient, R. B., has also supported the division of LTM into implicit and explicit memory. R. B. had specific lesions to the CA1 region of the hippocampus (Zola-Morgan, Squire & Amaral, 1986), and was found to have good general cognitive functioning, as measured by the Wechsler Adult Intelligence Scale (WAIS), but impaired explicit memory, as evidenced by his WMS score, which was 20 points lower than his WAIS score; in neurotypical patients these scores should be equivalent (Zola-Morgan et al., 1986). Like H. M., R. B. was found to have intact priming abilities (Experiment One, Case One; Graf, Shimamura & Squire, 1985), in the absence of functioning explicit memory. This finding suggested that the hippocampus was necessary for the normal functioning of explicit LTM, and magnetic resonance imaging (MRI) of H. M. revealed that many of his MTL structures were intact but that there was specific damage to the hippocampus (Corkin, Amaral, González, Johnson & Hyman, 1997). Therefore the hippocampus has been proposed to be necessary for the normal functioning of explicit memory abilities. Importantly, H. M. and R. B. both showed relatively intact retrospective explicit memory, as they were able to explicitly recall memories from their pasts (Scoville & Milner, 2000; Zola-Morgan et al., 1986). This suggested that

the storage of explicit memory is dissociable from the encoding of explicit memories, and it has been proposed that the frontal lobes may be the site involved in storing consolidated long-term memories (Shimamura, Janowsky & Squire, 1990). However, patients showing intact implicit memory abilities in the absence of explicit memory abilities, like H. M., R. B., and several others (see Graf, Squire & Mandler, 1984; Schacter, 1985; Shimamura, 1986) only provide evidence of a single dissociation between implicit and explicit memory. It is possible that explicit memory processes are simply more cognitively demanding of a single LTM system, and so are impaired in individuals with brain damage (Ellis & Young, 1996). However, Gabrieli, Fleischman, Keane, Reminger and Morrell (1995) reported that one patient, M. S., showed functioning explicit memory but impaired perceptual implicit memory following the removal of the right occipital lobe to treat epilepsy. A similar patient, L. H., was reported by Keane et al. (1995) who showed intact explicit memory performance but impaired implicit memory performance after sustaining bilateral occipital lobe lesions. This double dissociation suggests that implicit and explicit memory are independent LTM systems and not graded processes of a single LTM system, with explicit memory relying on the MTLs, and specifically the hippocampus, whilst perceptual-based implicit memory relies on the occipital lobes.

There is, however, the need for caution in experimental neuropsychology when formulating cognitive models, such as the hippocampal model of explicit memory, solely on evidence from clinical patients. As Capitani and Laiacona (1999) highlighted, clinical patients differ from controls in respect to age and education, the site of patient’s lesions cannot be controlled, and

care must be taken as the testing of single clinical patients can cause issues with statistical reliability. However, it has also been suggested that the use of groups of amnesic patients may be inappropriate for understanding specific deficits in cognitive systems, as patient's deficits may be treated as homogenous when they are not (Capitani & Laiacona, 1999). Therefore the finding of multiple single-cases, alongside group findings such as those from patients with TLE, has strengthened the notion that implicit and explicit memory are functionally and structurally dissociable. Additionally, studies of neurotypical patients in experimental neuropsychology, as already discussed, has supported the functional dissociation of implicit and explicit LTM. Further studies of neurotypical individuals, utilising neuroimaging techniques, have also supported the structural dissociations between these two types of LTM that were initially discovered through studies of clinical patients. Neuroimaging, such as positron emission tomography and functional MRI, provides fine-grained spatial information about the neural sites activated during tasks, and has been advocated by many researchers (e. g. Henson, 2006). Several neuroimaging studies have found that neurotypical participants show activation in the hippocampal and MTL regions during explicit memory tasks, whilst implicit memory shows activation in the motor, or perceptual areas involved in the original encoding of information (e. g. Eldridge, Knowlton, Furmanski, Bookheimer & Engel, 2000; Keane et al., 1995; Rauch et al., 1995; Schacter, Alpert, Savage, Rauch & Albert, 1996; Squire et al., 1992; see Gazzaniga, Ivry & Mangun, 2009). Additionally, electrophysiological measures of explicit and implicit memory, which provide more detailed information about the temporal course of neural activations than neuroimaging methods, but are much less

accurate at examining the specific neural sites of activation (Luck, 2005; Woodman & Luck, 2005), have similarly suggested that implicit and explicit memory are dissociable relying on structurally distinct neural areas (Rugg et al., 1998). Therefore, evidence from both clinical neuropsychological patients, and neurotypical individuals, has consistently suggested that explicit and implicit memory are both functionally and structurally dissociable systems of LTM. Importantly, clinical patients have been instrumental in supporting the divide of LTM into explicit and implicit memory, which emerged in experimental settings.

The studies discussed so far have considered one side of the relationship between clinical and experimental neuropsychology; the influence of clinical neuropsychological patients in experimental neuropsychological research investigating brain-behaviour relations. The relationship between clinical and experimental neuropsychology, however, appears to be one of mutual understanding, with each branch of neuropsychology influencing and aiding the other. The finding that memory-impaired individuals can have impaired explicit memory abilities but intact implicit memory has formed the basis of clinical rehabilitation approaches, which focus not on restoring memory functions but on alleviating memory deficits through residual learning in implicit memory (Hunkin & Parkin, 1995). As has been highlighted, several different amnesic patients have shown functioning implicit memory in the absence of explicit memory. Additionally, the same pattern is found in patients diagnosed with Alzheimer’s disease (AD). AD is the most common form of dementia and is characterised by explicit memory deficits in early-stages, caused by medial temporal lobe (MTL) degradation, and more

widespread cognitive and neural decline in later-stages (Alzheimer's Research Trust, 2010; Buckner 2004; Gazzaniga et al., 2009). Two rehabilitation methods will be discussed in relation to amnesic and AD patients.

One method, known as the vanishing cues (VC) method, was developed by Glisky, Schacter and Tulving (1986a). The VC method involves presenting participants with a word-stem, with as many letters as is needed to elicit the correct response. Over learning trials, letters are removed from the word-stem until the participant is able to produce the target word without any letter cues. The theory behind the VC method is that information is gradually encoded into implicit memory where it can then be used in the absence of explicit memory. Glisky, Schacter and Tulving (1986b) tested four patients with explicit memory deficits varying in severity and found that, through use of the VC method, the patients were able to learn complex computer commands and operations, albeit at a slower rate than neurotypical controls. These skills were considered important for the amnesic patients as it would allow them to programme computerised memory aids (Glisky et al., 1986b). Glisky et al. (1986b) proposed that the computer commands were encoded into the amnesic patients' implicit memory, where they could then be used to complete programming sentences. Additionally, Glisky et al. (1986a) reported that the knowledge learnt through the VC technique lasted over a 6-week interval and that there was evidence of the implicit knowledge being used outside of the domain it was learnt in, even though patients had difficulties in answering explicit questions about how to programme computers. The VC method has, however, been criticised by Hunkin and

Parkin (1995), who compared the VC technique to a standard rote learning method, and found that amnesic patients were able to learn equally as well through either method. In a second experiment Hunkin and Parkin modified the VC procedure so that it relied more exclusively on implicit memory, and found that participants recalled more of the computer-terms learnt through standard rote learning than through the modified VC technique. However, the VC technique led to the longer retention of information. Hunkin and Parkin suggested that the VC technique appeared to work best when used with participants with severe explicit memory impairments, impaired IQ and/or frontal lobe dysfunction, such as the deficits that may occur in late-stage AD (see Baddeley, Baddeley, Bucks & Wilcock, 2001; Gazzaniga et al., 2009), whilst rote learning appeared to lead to better performance in those with mild explicit memory deficits, where some explicit memory abilities remained. Hunkin and Parkin (1995) also criticised the VC method as it allows the encoding of errors, which once encoded into implicit memory are hard to correct (see Baddeley & Wilson, 1994; Squires, Hunkin & Parkin, 1997).

Another technique, known as Errorless Learning (EL), has been used for rehabilitating memory impaired individuals. Like the VC method, EL is based on the principle of intact implicit learning in memory-impaired participants, such as those with AD (Baddeley & Wilson, 1994). Importantly, unlike the VC method, EL does not allow the encoding of errors into implicit memory. Wilson, Baddeley, Evans and Shiel (1994) compared EL and errorful learning (EF) in memory-impaired patients. In the EL condition the patients were presented with a sentence, such as “ I’m thinking of a five-letter word

beginning with the letters CH, and the word is CHAIR. Please write it down". In the EF condition the patients were presented with a sentence, such as " I'm thinking of a five-letter word beginning with the letters TA, can you guess what the word might be?" Following a set time-limit or number of guesses, patients are told the right answer (TABLE) and asked to write it down. Amnesic patients showed learning of the words in the EL condition, but not the EF condition, as evidenced by the increased use of the words they had written down to complete word-stems, such as " TA_ _ _". This learning was attributed to intact implicit memory in the memory-impaired participants (Baddeley & Wilson, 1994; Wilson et al., 1994). Additionally, EL has been found to help AD patients to learn new face-name associations and information important for everyday functioning in the context of general mental deterioration (Clare et al., 2000), without affecting patient's well-being, through training stress (Clare, Wilson, Carter, Roth & Hodges, 2002). Recently, however, it has been suggested that EL may not tap implicit memory, but in fact utilises residual explicit memory abilities (see Clare et al., 2000; Hunkin, Squires, Parkin & Tidy, 1998), perhaps within a compensatory frontoparietal network when the MTLs are impaired, such as in TLE and AD (see Pariente et al., 2005). Nevertheless, although it is unclear exactly which memory system underlies the benefits of EL, this method was developed out of the experimental neuropsychological findings of dissociable implicit and explicit memory systems in clinical patients and neurotypical individuals, and the suggestion that implicit memory could allow the learning of new information in the absence of explicit memory. Clare et al. (2000) concluded that it is possible that the benefits of EL occur due to the facilitation of both residual explicit memory, and implicit memory.

Nonetheless, the EL technique has proved a useful method for teaching memory-impaired patients new information, and in their review Kessels and Haan (2003) reported that EL is a much more effective learning technique for memory-impaired participants than the VC method.

As has been shown, clinical neuropsychological patients were instrumental in dividing LTM into separate models of explicit and implicit memory, and this division has been acknowledged in clinical neuropsychology in the exploitation of residual memory abilities in memory-impaired patients. However, both implicit and explicit memory have been further subdivided. Explicit memory has been proposed to consist of an episodic store (memory for personal events) and a semantic store (memory for general and factual knowledge) (Tulving, 1972, 1995). Like the division of LTM into explicit and implicit memory, these further subdivisions of explicit memory are based on convergent evidence from experimental and neuroimaging studies of clinical patients and neurotypical individuals (e. g. Prince, Tsukiura & Cabeza, 2007; Rosenbaum et al., 2005; Vargha-Khadem et al., 1997). However, these further subdivisions of explicit memory, and the existence of implicit memory, have rarely been acknowledged in clinical neuropsychological assessments of early-stage AD (Spaan, Raajimakers & Jonker, 2003). The Diagnostic and Statistical Manual of Mental Disorders Fourth Edition (DSM-IV; American Psychiatric Association, 1994) defines AD related memory impairments as “ an impaired ability to learn new material or the forgetting of previously learnt material” (p. 134). Spaan et al. (2003) highlighted that this means that clinical tests, which are based on this definition, have considered AD related memory impairments in relation to a single LTM

system. Spaan et al. highlighted that the clinical tests used in diagnosing AD focus exclusively on testing episodic memory. Episodic memory has been found to be severely degraded in AD (Eslinger & Damasio, 1986; Greene, Baddeley & Hodges, 1996 Koivisto, Portin & Rinne, 1996), but has also been found to be degraded in healthy ageing older adults (Jelicic, 1996; Hudson & Roberts, 2007). Spaan et al. (2003) highlighted that in early-stage AD the difference between episodic memory functioning in healthy individuals and AD patients may not be distinguishable. Early-stage AD has, however, also been associated with impairments in semantic memory (Beatty, Testa, English & Winn, 1997; Weingarter, Kawas, Rawlings & Shapiro, 1993), and these impairments are qualitatively different to those that occur in healthy ageing. Spaan et al. (2003) suggested that the use of semantic memory tests may provide a useful means of detecting early-stage AD, and that although some aspects of semantic memory are measured in clinical neuropsychological tests (e. g. the verbal intelligence subtests of the WAIS-Revised), the results of these tests are rarely interpreted as measures of semantic memory. Similarly, measures of implicit memory may also provide a means of detecting the cognitive changes associated with early-stage AD. Hudson and Roberts (2007) used the PDP, with guided instructions making the procedure easier for memory-impaired individuals (Stern, McNaught-Davis & Barker, 2003), and found explicit memory to be severely impaired in individuals with AD compared to healthy age-matched controls, whilst implicit memory was also significantly impaired, but to a much lesser extent than explicit memory. Therefore the PDP may provide a useful means for differentiating early-stage AD from healthy ageing, through measuring declines in implicit memory which do not appear to occur in healthy ageing

(see Hudson, 2008). However, more extensive testing using the PDP is needed, and this approach would still need to be combined with more extensive memory testing, including measures of semantic memory. Therefore, as Spaan et al. (2003) concluded, the theoretical knowledge about the structure of LTM discovered through experimental neuropsychology is not yet well integrated into the clinical assessment of AD, and examination of semantic and implicit memory abilities in clinical assessments may provide a useful means for the early detection of AD, which is crucial for the most effective treatment and rehabilitation techniques.

In conclusion, experimental and clinical neuropsychology are separate but interdependent domains of neuroscience, with clinical patients informing models of normal cognitive functioning, and these models forming the basis of clinical rehabilitation methods. However, Oscar-Berman (1989) highlighted that clinical and experimental neuropsychology have not influenced each other equally, with clinical neuropsychological patients having a greater impact on experimental neuropsychology, than experimental neuropsychological findings impacting clinical neuropsychology. This appears to be the case in the study of LTM, where clinical neuropsychological testing has yet to fully embrace the experimental neuropsychological notion of multiple LTM stores in the diagnosis of early-stage AD. Future research must involve clinical neuropsychology acknowledging the multiple systems of LTM, as well as experimental and clinical neuropsychology further investigating the exact memory systems utilised in clinical memory rehabilitation techniques, such as EL. Nonetheless, the relationship between clinical and experimental neuropsychology has mostly been one of

interdependence, and this relationship has, and will continue to be, beneficial for both neuropsychology’s understanding of LTM and for the memory-impaired patients that are studied.