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## The application of cognitive event-related brain potentials (ERPs) in language-impaired individuals: review and case studies

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### Abstract

There is a substantial body of basic research that has utilized ERPs to investigate the neurological basis of cognition. This research has, in turn, led to the development of practical applications of cognitive ERPs in patient populations. In particular, recent work has focused on the development of ERP-based assessment measures for the neuropsychological assessment of dyslexia and language impairments secondary to stroke. This review describes the innovative assessment methods program (IAMP), an initiative to utilize ERPs for a neuropsychological assessment of patients who cannot be evaluated by traditional methods. The success of this program has demonstrated that ERPs can be used to reliably evaluate an individual's reading and speech comprehension abilities, independent of behavioral and speech production impediments. In contrast to traditional neuropsychological assessment, these ERP methods can discern the cognitive strategies used by an individual to perform a task. © 2000 Elsevier Science B.V. All rights reserved.

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## 1. Introduction

Patient assessment is the cornerstone of the caregiver's choice of treatment, the process of therapeutic intervention, treatment monitoring and thus, ultimately, patient outcome. Evoked potentials (EPs) in response to simple auditory, visual or somatosensory stimuli have long been used to evaluate sensory function in patients (Chiappa, 1997). The success of this approach has led to the standard use of EPs in a variety of clinical contexts. The perception of EPs is that they reflect hardwired systems, and thus, are themselves reliable and invariant. It has long been held that while sensory EPs are reliable enough to be used in clinical contexts, cognitive event-related potentials (ERP) may be too variable to be clinically useful. Another criticism has been that differences in ERPs between cognitive tasks can best be demonstrated with grand averaged waveforms and are less reliably demonstrated at an individual subject level. Simply put, this is a dated and fundamentally incorrect belief. ERPs provide an essential neurophysiological index of mental functions generally, and can be utilized to assess those functions following neurological insult on an individual subject basis. Connolly and D'Arcy (2000) have reviewed the development of and normative data for a series of ERP-based assessment measures of language function. This work has demonstrated that various neuropsychological tests can be adapted for computer presentations and simultaneous ERP recording. The presence or absence of the cognitive function(s) in question can be determined by the existence of a predicted ERP component, which has been shown previously to reflect that function.

Why is the linking of ERP components to neuropsychological tests important? The ability to establish levels of intellectual function in patients who have experienced neurotrauma is essential for their assessment and treatment. However, a common consequence of neurological insult is impaired communication abilities (Marquardsen, 1969; Wade et al., 1986; Enderby and Philipp, 1987; Enderby et al., 1987; Morse and Montgomery, 1992; Pedersen et al., 1995). Impaired communication frequently hinders the clinician's

ability to assess intellectual function, making neuropsychological testing difficult, unreliable or totally impossible. Thus, the availability of an assessment measure that functions independently of communication disabilities would provide invaluable information about intellectual function when traditional measures fail. It is possible to use ERPs in order to fulfill that role. Furthermore, when acquired in a psychometrically defined context (i.e. using a neuropsychological test), the level of inference required to interpret a particular ERP waveform is minimal. For instance, in a language comprehension context, the failure to emit a P300 to a correct definition of a target word in a vocabulary test (Connolly et al., 2000,b) or a PMN/N400 to a spoken word incorrectly describing an accompanying picture in a picture–vocabulary test (Byrne et al., 1995a,b; Connolly et al., 1995a) reflects a failure to comprehend the meaning of the target words. Confirmation of this interpretation has been demonstrated when vocabulary levels tested exceed the individual's knowledge level and ERP components no longer differentiate correct from incorrect definitions.

Aside from the applications that ERP-based measures have for assessing individuals with language impairments, these methods also have widespread implications for assessing attention, memory, perception, and levels of consciousness. In fact, any cognitive function currently measured with neuropsychological tests may be amenable to assessment with ERPs. The primary advantage of using ERP measures in addition to traditional neuropsychological measures is that the former provides information about the cognitive strategies used in performing a given task.

This paper presents a review of this work and is divided into two sections. In the first section (Section 2), a subset of the neuropsychological tests that were adapted for computer presentation and simultaneous recording of ERPs and the ERP components associated with normal performance of those tests have been briefly reviewed. Please refer to Table 1 for a summary of these studies, and for a more detailed description of test adaptation and normative work, the interested reader is referred to Connolly and D'Arcy

Table 1

The table provides a summary of normative data from the adapted tests, an overview of the relevant cognitive processes, and a list of the associated ERP components (see text for further details)

Paradigm	Cognition	Component(s)	References
Psycholinguistic N400 Visual <i>N</i> = 20 Age <i>M</i> = 21 Range = 19–24	Semantic processing	N400	Connolly et al., 1995b
Auditory <i>N</i> = 20 Age: <i>M</i> = 21 Range = 18–43	Phonological and semantic processing	PMN, N400	Connolly and Phillips, 1994
Computerized PPVT-R Adults <i>N</i> = 12 Age: <i>M</i> = 27 Range = 23–34 Youth <i>N</i> = 3 Age: <i>M</i> = 17.6 Range = 16–18 Children <i>N</i> = 15) Age: <i>M</i> = 10.3 S.D. = 0.6	Receptive vocabulary level	PMN, N400 P300	Byrne et al., 1995a,b Connolly et al., 1995a
Computerized PALPA Adults <i>N</i> = 23 Age: <i>M</i> = 22.9 S.D. = 4.2	Reading comprehension	P300	D'Arcy et al., 2000b
Computerized Token Test Adults <i>N</i> = 27 Age: <i>M</i> = 23.2 S.D. = 5.8	Speech comprehension; attention and phonology	P300, N2b	D'Arcy and Connolly, 1999 D'Arcy et al., 2000a

(2000). The purpose of the second section of this article (Section 3) was to highlight some of the recent applications of these tests in the evaluation of impaired language functions in dyslexic readers and stroke patients.

## 2. Normative ERP results in computerized neuropsychological tests

### 2.1. Peabody picture vocabulary test — revised (PPVT-R)

The PPVT-R is a well-established assessment

tool for evaluating vocabulary knowledge (Dunn and Dunn, 1981). The computer adaptation of the PPVT-R has maintained all critical aspects of the original test by dividing it into three levels of difficulty. For each item, participants viewed a picture paired with a spoken word (that was congruent/incongruent), and the ERP recordings were time-locked to the onset of the spoken word. Fig. 1a represents the sequence and time course of stimulus presentation. The development of this version of the test was directed at establishing receptive vocabulary ERP norms in adults and children (Byrne et al., 1995a,b; Connolly et al., 1995a). Also, these initial studies compared per-

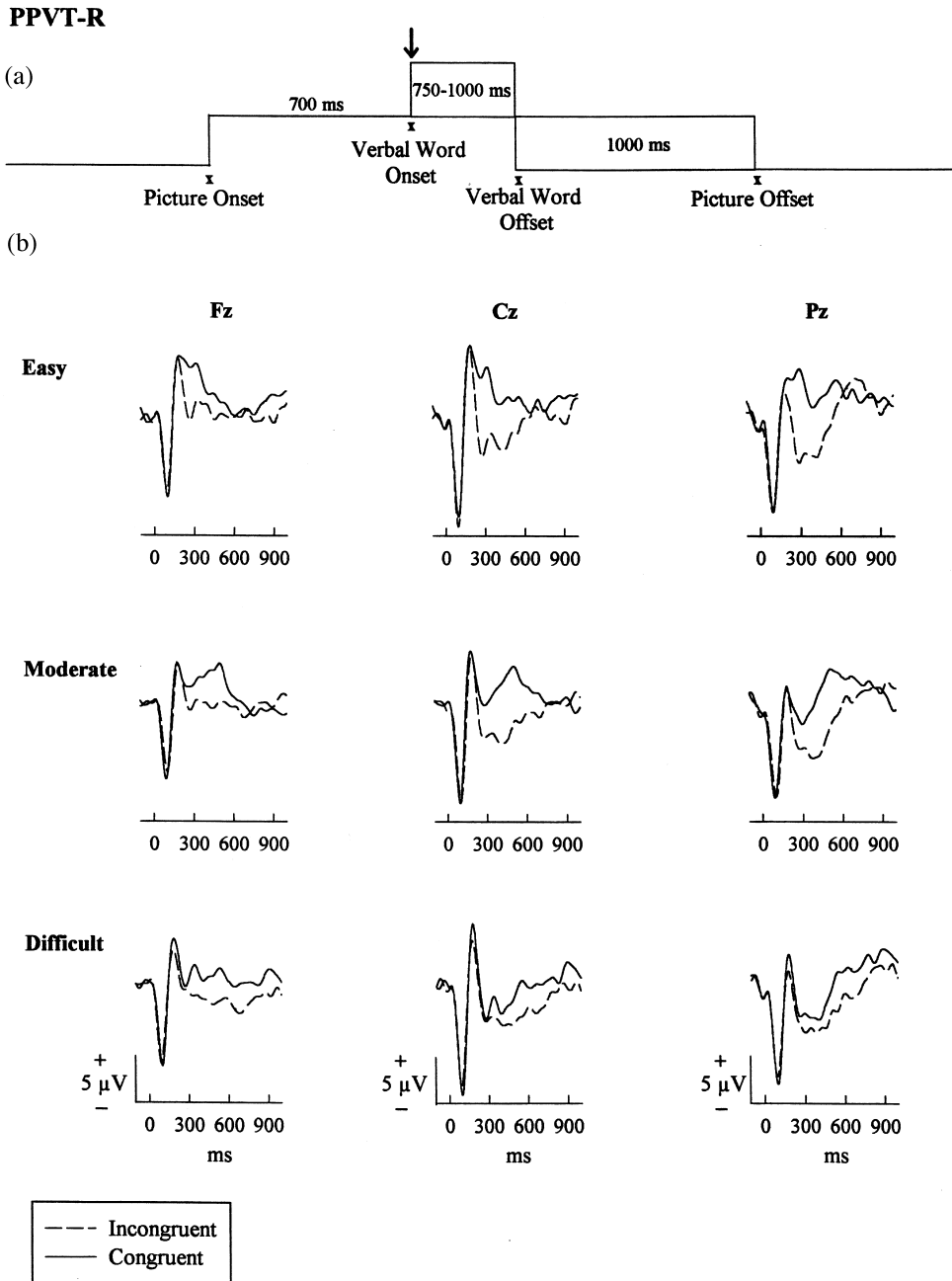


Fig. 1. (a) Schematic of the computerized PPVT-R representing the time course of stimulus presentation. Participants were required to judge whether or not a spoken word matched the picture. ERPs were time-locked to the verbal word onset (arrow). (b) Grand average waveforms recorded at Fz, Cz, and Pz. The three levels corresponded to gradients of difficulty, such that 'easy' represented a pre-school vocabulary level, 'moderate' represented a child vocabulary level, and 'difficult' represented an adult vocabulary level. ERPs to incongruent picture-word pairs were differentiated from those to congruent picture-word pairs on the basis of the PMN and N400. Time in milliseconds (ms) is represented on the horizontal axis and amplitude in microvolts ( $\mu\text{V}$ ) on the vertical axis. Positive is up. (Figure adapted from Connolly et al., 1995a)

formance on the computerized version with that on the standard version, to establish that the adapted version had not violated the test's psychometric properties.

As Fig. 1b depicts, two distinct components were generated to the incongruent spoken words. First, the phonological mismatch negativity (PMN) was elicited when the initial phoneme mismatched that of the expected initial phoneme of the spoken word. Secondly, the N400 was elicited to violations in semantic expectancy. The PMN likely reflects sub-lexical spoken word processing, while the N400 reflects post-lexical processing in both speech processing and reading (Connolly and Phillips, 1994; Connolly et al., 1995b; Brink et al., 1999; Hagoort and Brown, 1999). Thus, it is possible to measure not only comprehension, but also the stages of linguistic processing in patients on the basis of ERPs (and independent of behavior). More importantly, these effects were seen only if the word was within the individual's vocabulary knowledge level. If the participant was tested at vocabulary levels beyond their knowledge, then the waveforms failed to differentiate. Also, differential patterns could be established at an individual subject level; an essential component of the process if the measures are to be used clinically.

The PPVT-R adaptation represented one of the first applications of the IAMP in a clinical setting. A single case of an individual with cerebral palsy was used to evaluate whether ERPs could adequately track receptive vocabulary levels in such a patient. Briefly, data were recorded from a patient with cerebral palsy (CP) and three matched control subjects using the computer-adapted PPVT-R (Byrne et al., 1995a). As was anticipated, the healthy controls showed clear N400 differentiation at lower vocabulary levels, but did not do so at the higher level vocabulary levels because the words were beyond their knowledge levels and they were unable to judge when a word was incongruent to its accompanying picture. These findings were confirmed with their performance on the alternate version of the standard test. Significantly, the CP patient demonstrated precisely the same patterns as the matched

controls on both the ERP computerized test and on the standard test.

## 2.2. Psycholinguistic assessments of language processing in aphasia (PALPA)

The written sentence comprehension section (Test 56) of the PALPA represents a test of sentence-reading comprehension that was designed from a cognitive neuropsychological, theory-driven orientation, to not only serve as a clinical tool, but also as a research device (Kay et al., 1992, 1996). The test assesses reading comprehension using a picture–sentence matching task. The format of the test uses a set of three pictures accompanied by a sentence that describes only one of them. The entire 60 picture–sentence sets in the standard test were adapted for computer presentation and ERP recordings (D'Arcy et al., 2000b). The computerized version of the test used a study phase/test phase format. In the study phase, participants saw a set of three pictures and the accompanying sentence with the instruction to read the sentence and decide which picture it correctly described. The pictures and sentence went off the screen and were followed by the presentation of each picture separately. ERPs were recorded for each picture presentation.

As Fig. 2a illustrates, correct pictures were differentiated from incorrect pictures on the basis of a P300 component. The P300 is an extensively investigated positive-going ERP component that has a variable latency depending on the complexity of the eliciting task and the processing speed of the individual. The P300 is conceptualized as reflecting a memory updating process in response to stimulus-driven changes in memory representations (Polich and Kok, 1995). Picton (1992) has observed that, amongst other things, the P300 was able to determine whether an individual was processing stimuli.

The parietally distributed P300 following correct, but not incorrect pictures, was interpreted to reflect a successful performance on the PALPA. Again, the critical issue was the test's utility at the individual participant level. The P300 differentiated correct from incorrect pictures at the individual participant level with 91.3% accuracy.

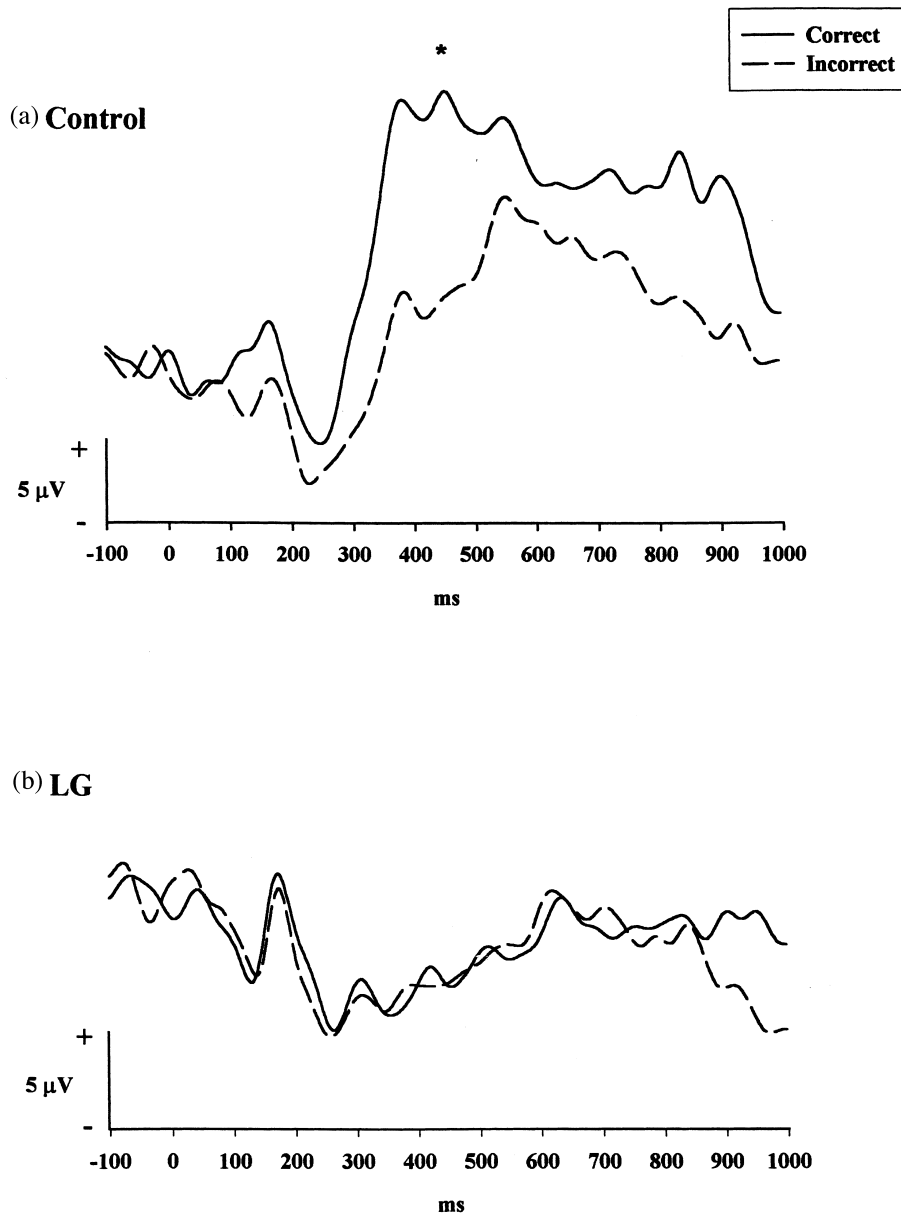


Fig. 2. (a) ERPs obtained from a representative participant while selecting the picture that corresponded with a written sentence (Pz). There was a significantly larger P300 response (asterisk) to correct pictures than to incorrect pictures. (b) Individual ERPs recorded from LG, a dyslexic participant, in which no differentiation between conditions was apparent (Pz). All other details as in Fig. 1. (Figure adapted from D'Arcy et al., 2000b)

In addition, participants' ( $N = 23$ ) performances on the standard PALPA and the computerized version were comparable with accuracy rates of 97.4 and 93.5%, respectively. These findings compare favorably with the norms provided by the test authors of 94.7%.

The differential response pattern observed in the PALPA could be isolated further in reduced-average (5-trial) waveforms within an individual. Data from a subset of participants ( $N = 10$ ) were examined using event-resolution imaging (ERI; Newman et al., 1999; Newman et al., in prepara-

tion). Briefly, this technique formed response templates based on time, frequency, and spatial distribution for correct and incorrect trials. The resulting templates could then be applied to new data sets formed with low numbers of trials. The mean total accuracy, sensitivity, and specificity levels for the five trial average classification processes were 72.9% (12.2), 77.9% (12.0), and 74.6% (15.9), respectively. Thus, when a trial contained P300 activity (i.e. a correct trial), ERI accurately detected and classified this trial as correct, 77.9% of the time. Equally, when an epoch did not contain P300 activity (i.e. an incorrect trial), the trial was accurately classified as being incorrect 74.6% of the time. The ability of ERI to discriminate smaller sets of trials than what is currently capable with traditional averaging, offers the potential to more accurately denote trial types and gradients of difficulty within computerized neuropsychological tests.

### 2.3. *Token Test*

The Token Test is used widely in neuropsychological contexts to evaluate speech comprehension in individuals (Boller and Vignolo, 1966; De Renzi and Vignolo, 1962; Lezak, 1995). The test's status as a gold standard for assessing comprehension made it ideal for computer adaptation and simultaneous ERP recording (D'Arcy and Connolly, 1999). In the traditionally administered test, an array of geometric shapes is placed in front of the patient and he/she is instructed to, for example, 'touch the green circle' or 'touch the black circle with the red square.' For the purposes of the ERP testing, the usual test procedure was reversed. The computerized Token Test (CTT) presented an array of colored geometric shapes on a computer screen and an animated pointer moved amongst the shapes touching either one or two shapes. A digitized spoken sentence, describing the previous animation incorrectly or correctly (0.5 probability) followed this sequence. Participants were instructed to watch the animation, listen to the spoken description and indicate behaviorally whether the description was correct or incorrect. The incorrect spoken description contained one word that did not match the ani-

mation. ERPs were recorded at the onset of this word. Thus, for example, if the pointer had touched a black square, the description may have said either 'black circle' (incorrect) or 'black square' (correct). The mismatching words could occur in either the shape word or the color word.

Also, as usual, a version of the Token Test (the 'short version', De Renzi and Faglioni, 1978) was administered to all participants in order to evaluate their performance on the computerized version with the standard version administered traditionally. Performance on the standard and computerized test proved to be comparable, with percentage correct scores of 97.1 and 96.8%, respectively. These values compared favorably with other data for normal adult populations of 98.7% (Spren and Strauss, 1991).

ERPs were found to differentiate incorrect and correct spoken descriptions of the animations seen on the CTT (D'Arcy and Connolly, 1999). Centro-parietal P300 responses were seen at approximately 500 ms after the presentation of the incorrect verbal description. The delayed latency reflected the complexity of the processing required to complete the task. Such cognitive processing is, by nature, variable (Gevins and Cutillo, 1986) and reflects a variety of functions, not least of which is stimulus evaluation time (Pritchard, 1981). Also, the processing of a speech signal takes place over a period of time, contributing further to the delay in the P300 latency. The P300 differentiation between incorrect and correct descriptions was seen reliably in over 92% of the participants, confirming the utility of this procedure at the single case level.

Participants performed the test in a 'target detection' manner that required speech comprehension abilities and attention (D'Arcy and Connolly, 1999; D'Arcy et al., 1999, 2000a). Furthermore, it has recently been reported that the N2b<sup>1</sup> can be elicited following a deviation in an elaborate speech processing task, demonstrating that this component is also sensitive to violations

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<sup>1</sup>The N2b is associated with voluntary attentional mechanisms used to detect stimulus deviance in processing sensory and cognitive stimuli (D'Arcy et al., 2000a).

in an active template formed from sensory processes (Ritter et al., 1992; Näätänen, 1995) and cognitive processes (D'Arcy et al., 2000a). Additionally, the authors speculated that the cognitive template was formulated on the basis of phonological working memory (Baddeley, 1992), which maintained and analyzed the visuospatial information from the previous animation. With respect to clinical applications, these findings demonstrated that in many of the computerized adaptations of neuropsychological tests, more than one ERP component differentiates correct from incorrect trials (see also, Connolly et al., 1999a). Furthermore, and of particular importance, these findings demonstrated that, by utilizing well-known relationships between ERP components and cognition, the manner in which an individual performs a neuropsychological task can be established.

#### 2.4. Psycholinguistic N400 paradigm

This experimental paradigm has been used in a variety of studies over the last 5 years (e.g. Connolly et al., 1995b; Helenius et al., 1998, 1999). The initial experiment using this design determined that the PMN and N400 were, in fact, distinct waveforms representing distinct language-related functions (Connolly and Phillips, 1994). The design used four conditions that varied along both phonological and semantic dimensions by manipulating the terminal words of contextually-constrained sentences. One condition involved the use of a sentence-terminal word that was the expected, semantically correct ending: 'The piano was out of tune.' The resulting ERP showed only a large, slowly developing positivity with no indication of either the PMN or N400. A second condition used sentences ending with a word that violated semantic expectancy and has an initial phoneme that is also unexpected: 'Joan fed her baby some warm nose' (milk being the expected word) produces both a PMN and a N400 in response to the terminal word. The PMN was seen in response to the initial phoneme mismatching the expected initial phoneme of the word milk, while the N400 reflected the semantic inappropriateness of the word. The remaining two

conditions are those that were designed to produce a double dissociation between the PMN and N400. Thus, 'The gambler had a bad streak of luggage' (luck being the expected word) resulted in a N400 with no preceding PMN because the word presented (luggage) shared its initial phoneme with the expected word (luck) but was semantically inappropriate to the sentence context. The final sentence type 'The pigs wallowed in the pen' (mud being the expected word) had an initial phoneme that mismatched context-driven expectations but was, in fact, semantically acceptable. Thus, the terminal words in these sentences produced a PMN but no subsequent N400.

The preceding section has provided an overview of a selection of paradigms that can be used to evaluate cognitive functions. In the Section 3, these paradigms are utilized in a series of individuals with language impairments (dyslexia and stroke) selected to demonstrate the efficacy of the IAMP and profile its use of ERPs as neurophysiological indices of cognition.

### 3. ERP results for clinical populations with language impairments

#### 3.1. Dyslexia

Recent work has utilized various neuroimaging techniques to examine language processing in dyslexic readers. Helenius et al. (1999) used the psycholinguistic N400 paradigm (Connolly et al., 1995b) to record event-related magnetic fields (ERMF) and ERPs in normal and dyslexic readers and to examine differences in the spatio-temporal characteristics of the N400m<sup>2</sup>. While a N400m was observed for both groups with no significant difference in the spatial distributions, the dyslexic readers showed differences in the timing and the strength of activation. In particular, the N400 response was delayed by ~ 100 ms and the amplitude was reduced (this reduction was especially noticeable following orthographic manipulations). Accordingly, the authors hy-

<sup>2</sup>The N400m is the magnetic equivalent of the N400.



pothesized that the dyslexic subjects were more reliant on sublexical word recognition (i.e. orthographic analysis) and, thus, may have utilized a smaller or less synchronous neural population during whole word semantic analysis. While the localization of N400m sources to the left superior temporal gyrus was similar for both groups, the pattern was much less distributed for the dyslexics. These results were relevant to data obtained in two independent case studies, described below, which outlined ERP manifestations of atypical language function and related fMRI findings.

### 3.2. Case study: LG

In research that used ERPs for the assessment of reading (PALPA) and speech comprehension (CTT), the examination of neural responses in the case study, LG, provided preliminary evidence for the sensitivity of ERPs to subtle developmental difficulties with reading (unpublished data). LG, a third year university undergraduate, was diagnosed with a learning disability at the age of eight and reported ongoing difficulties with reading, but not speech comprehension. Prior to university, he had received special training for his reading difficulties. In light of these reading-specific problems, it was predicted that his ERPs on the PALPA would be abnormal, but the expected differentiation (i.e. normal) would occur on the CTT.

Recall that the ERPs for healthy controls reliably differentiated correct and incorrect test items on the basis of the P300 response for both the PALPA and the CTT paradigms. In contrast, Fig. 2b illustrates that LG showed no observable differentiation between the correct and incorrect test items on the PALPA. Further support that the waveforms failed to differentiate conditions was found using a finer-grained signal analysis with ERI (Newman et al., 1999; Newman et al., in preparation). The analysis determined that 100% of correct trials were classified as being incorrect trials (i.e. no differentiating signal could be modeled). However, it was clear that he was processing the stimuli because the N1–P2–N2 complex was clearly identifiable and, of particular importance, his behavioral scores were perfect. Inter-

estingly, his ERPs on the CTT differentiated the incorrect and correct test items and the response pattern was comparable to that of other subjects. Thus, only the ERP findings corroborated LG's initial report of difficulties with reading, but not speech comprehension.

Two important observations resulted from LG's performance and ERP findings. First, his behavioral scores were high, and yet on the PALPA the ERPs did not concur with the behavioral results. This discrepancy did not indicate that the ERPs were unreliable (as the measure has been proven in matched controls and the waveforms indicated intact stimulus processing), but instead suggested that LG performed this reading task (i.e. identified the correct test items) in a different manner than normal readers. D'Arcy et al. (2000b) have stated that the normal readers were capable of formulating accurate linguistic representations and then subsequently identifying the correct test item that matched this linguistic representation through recognition memory processes. This process was inferred through the examination of the task demands and the ERP waveform, specifically the presence of the P300.

It is likely that the observed absence of the P300 response for LG indicated a significantly different processing strategy. For instance, if LG experienced difficulty in either the formulation or maintenance of linguistic representations, then the impaired linguistic representation may have required a more intensive item-by-item decision process instead of a recognition process directed at identifying a previously selected picture. Thus, this item-by-item decision process would be directed at discriminating both the correct and incorrect test items during the data collection phase. In support of this interpretation, LG showed a strong negative-going waveform (200–500 ms period) in both experimental conditions. This negative-going waveform was consistent with the ERP patterns hypothesized to reflect active linguistic processing during the computerized PPVT-R (Byrne et al., 1995a,b; Connolly et al., 1995a).

The second important observation concerned the sensitivity of ERP responses during the assessment of cognitive functions. In the case of LG, the results from the neuropsychological test

did not reflect any difficulties with reading, and using these results alone it would not have been possible to identify the anomalies associated with this case. It was only when ERPs were simultaneously recorded, that it was possible to detect differences secondary to a reading disability. However, an important caveat exists; these findings were based on a single case study and further evidence for these ERP assessment techniques must be obtained from other high-functioning dyslexic individuals.

### 3.3. Case study: BP

Recently, ERPs and fMRI have been used to evaluate reading abilities in a high-functioning individual (BP) with profound dyslexia. Traditional neuropsychological testing revealed that BP had a severe phonological impairment as measured by non-word reading and phoneme deletion tasks. Despite this reading-related impairment, BP had developed successful compensatory strategies as demonstrated by his ability to obtain a Master's degree.

Using ERPs, BP was tested on the psycholinguistic N400 paradigm (Connolly et al., 1995b), the computerized PALPA, and the CTT. Fig. 3 depicts BP's performance on each of these tests as compared to a representative control participant. On the psycholinguistic N400 paradigm, BP showed no differentiation whatsoever following the presentation of anomalous terminal words in which the orthographic/phonological and/or semantic features were unexpected. The failure to observe a N400 suggested that BP had a reduced capacity to process the lexical/sub-lexical features of the terminal word and had difficulty integrating it into the context of the preceding sentence. In support of this interpretation, BP also showed no ERP differentiation to the PALPA test items. ERI analysis found that 83% of incorrect trials were classified as correct trials, indicating that there was insufficient signal differentiation between the two conditions. Indeed, the findings in this case replicated the previous case study in that BP's behavioral performance was accurate. In addition, when BP was tested on

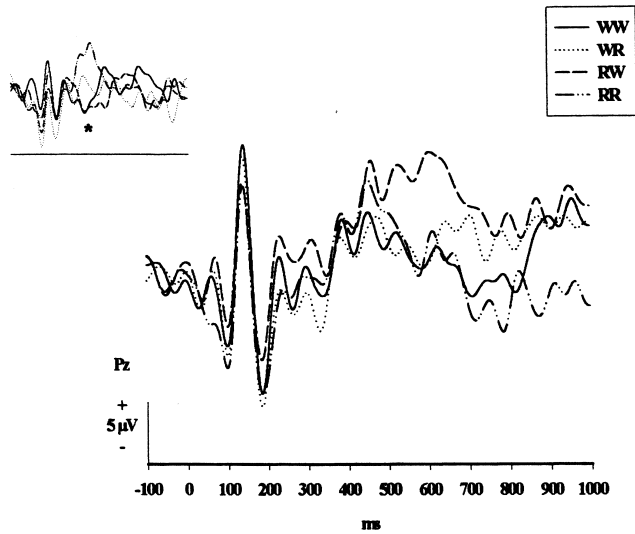
speech comprehension with the CTT, there was an observable differentiation in the waveforms (again, similar to LG's results). The only difference between the two case studies involved the morphology of the waveforms. In the case of BP, there appeared to be P300 responses in both conditions, whereas, in LG's data there was a sustained negativity. Nonetheless, in both cases, it was likely that the lack of expected differentiation resulted from an item-by-item decision strategy (making all test items equally salient).

As mentioned previously, both ERP and fMRI data were collected for BP. The fMRI (1.5 T) provided a neuroanatomical backdrop for the ERP components used in language assessment with the psycholinguistic N400 paradigm. Fig. 4a highlights the contrasting pattern of activation observed between a representative subject and BP. In normal readers, two key regions were activated during reading in general: (1) the visual cortex (striate and extra striate); and (2) Broca's area. The left perisylvian region (angular gyrus), left posterior parietal regions, posterior cingulate gyri, and frontal areas were particularly sensitive to the psycholinguistic properties of the terminal word (D'Arcy et al., 1999; Connolly et al., in preparation). In contrast, the reading-related profile obtained from BP differed markedly. While BP did show activation in the visual cortex, the remaining regions identified in controls were not activated. Instead, robust activation was observed centered in the sylvian fissure (anterior to the primary auditory cortex) which, while bilateral, was stronger in the left hemisphere. Fig. 4b demonstrates the overlap between active regions identified with fMRI and MEG N400m dipole solutions (Helenius et al., 1999) for high functioning dyslexics. Considering both the ERP and fMRI results, it was likely that BP utilized a different reading strategy, which in turn was evidenced by differences in neural processing and the anatomical regions of activation.

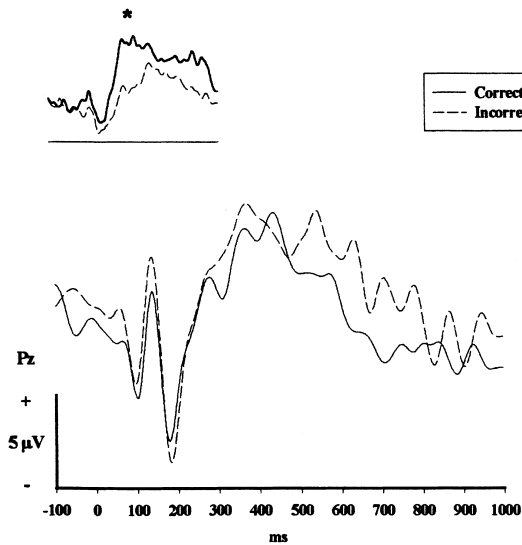
### 3.4. Stroke

As the objective of the IAMP was to use ERP-based measures to assess non-communicative

(a) **Psycholinguistic N400 paradigm**



(b) **PALPA**



(c) **CTT**

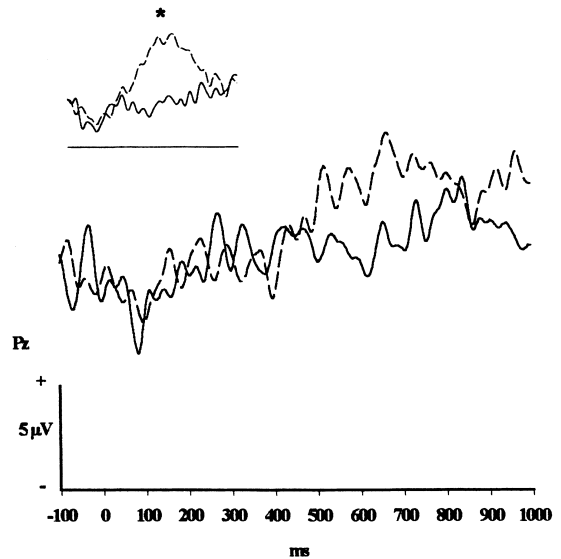
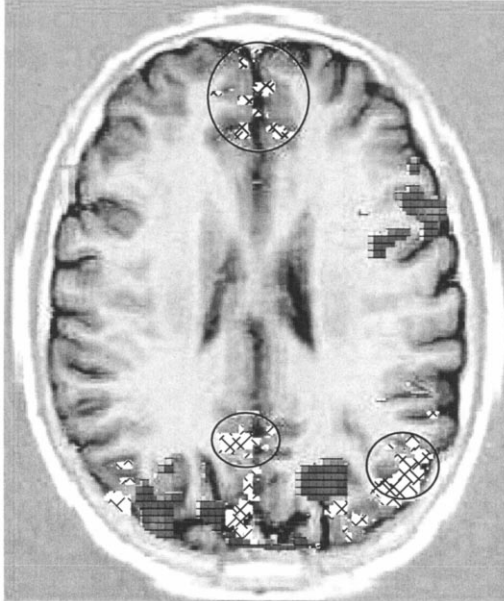


Fig. 3. Individual ERPs at Pz obtained from BP, a dyslexic on the psycholinguistic N400 paradigm (a), the PALPA (b), and the CTT (c). Individual ERPs obtained from representative control participants on each of the respective tests are inserted for comparison. (a) BP failed to show an observable N400 to anomalous sentence-ending words. Waveforms corresponding to each of the four conditions are represented as follows: semantically congruent/phonologically expected (RR), semantically congruent/phonologically unexpected (WR), semantically incongruent/phonologically expected (RW), semantically incongruent/phonologically unexpected (WW). (b) BP showed no differentiation on the PALPA (P300 in both conditions). In contrast, a control participant showed a larger P300 in the correct condition. (c) On the CTT, ERPs differentiated incorrect from correct spoken descriptions of the animation sequence for both the control participant and BP. The P300 is denoted by an asterisk. All other details as in Fig. 1.

### A. fMRI - Psycholinguistic N400 paradigm

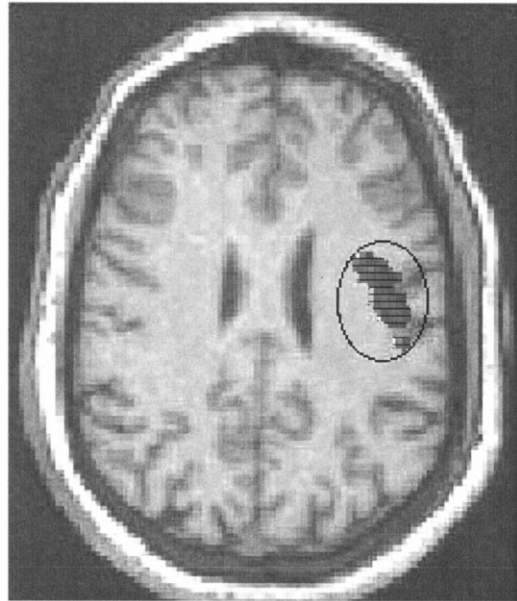
Control



Right

Left

BP

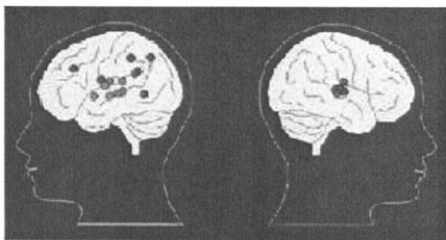


Right

Left

### B. MEG - N400

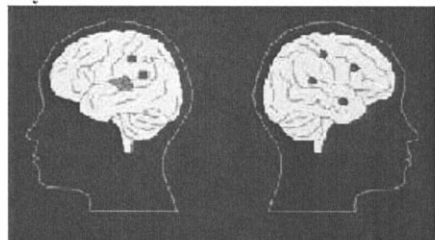
Controls



Left

Right

Dyslexics



Left

Right

Fig. 4. (a) Functional MRI (blood oxygen level dependent contrasts at 1.5 T) depicts the regions activated during the psycholinguistic N400 paradigm. For a normal reader, robust reading-related (gray checker board) activation was observed in the visual cortices (striate and extrastriate) and Broca's area. In addition, activation related to evaluating the terminal word (cross hatched) was observed in the left angular gyrus, posterior cingulate gyri, and frontal regions (circles). In contrast, BP showed predominant activation in the visual cortex and the left sylvian fissure region (circle). Note that fMRI images are presented radiologically with an AC-PC orientation for the control and a horizontal orientation for BP (i.e. visual cortex is not imaged for BP). (b) Source localization of N400m dipoles in the left and right hemispheres for controls and dyslexics, from the same paradigm. Both the controls and dyslexics showed activation in the left superior temporal gyrus, though sources for the dyslexics were more focused. (Figure adapted from Helenius et al., 1999).

patient populations, a group of stroke patients became the focus of recent work. The patients described below were assessed using the Boston Diagnostic Aphasia Examination (Goodglass and Kaplan, 1983).

Patient 1 was a 53-year-old woman who suffered a left hemisphere stroke 1 month prior to her participation in the study. She showed mild expressive aphasia and apraxic speech, the combination of which presented as stuttering. Her reading comprehension was unimpaired at the sentence level, but her reading became laborious as the complexity of material increased.

Patient 2 was a 71-year-old man who suffered a left lacunar stroke 1 month prior to testing. He showed mild impairments on measures of oral expression, reading comprehension, and fluency, and severe impairments on measures of written expression. He also presented with mild dysarthria, mild word finding difficulties and difficulty attending to lengthy text during reading.

Patient 3 was a 60-year-old female who suffered a left hemispheric stroke 2 months prior to testing. Of the three patients tested, she exhibited the most language-based difficulties. She presented with moderate expressive, and mild to moderate receptive difficulties. She showed perseverations, paraphasias, neologisms, and decreased meaningfulness in the content of her output. While her auditory comprehension was unimpaired at the sentence level, her reading comprehension was moderately impaired at the sentence level.

The three patients were tested on the standard and computerized versions of the PALPA. Data from these patients were compared to a group of elderly controls, which like young adults (D'Arcy et al., 2000b), showed ERP differentiation as indexed by a P300 to correct pictures. Importantly, the controls demonstrated waveform differentiation regardless of whether or not they provided a behavioral response.

Scores obtained on the standard version of the PALPA were 83.3, 90, and 76.7% for patients 1, 2 and 3, respectively. The mean score for the elderly controls was 97%, indicating that all patients performed more than 1 S.D. below the mean of the control group. As shown in Fig. 5, the ERPs

of patients 1 and 2 on the computerized version showed a differentiation between correct and incorrect conditions, while patient 3 showed no significant differentiation. Furthermore, the amplitude of the P300 to correct pictures matched the pattern of patient performance on the standard PALPA, i.e. patient 2, who was most accurate on the behavioral PALPA, exhibited the largest P300. Patient 1, whose behavioral score was intermediate between patients 2 and 3, demonstrated reduced P300 activity in comparison to patient 2. Finally, patient 3, who had the lowest behavioral score, showed no evidence of P300 activity.

Two important points about these results should be highlighted. Firstly, ERPs were able to index comprehension of the written text, irrespective of whether a behavioral response was required. The ability to record ERPs to stimuli that invoked cognitive processing regardless of the presence/absence of behavioral responding enables this technique's use with non-communicative and 'difficult to assess' individuals (see also Connolly et al., 1999b). The second important point is that ERP differentiation has been shown to occur, not only in healthy, young undergraduate volunteers, but also in patients of widely differing ages who have a variety of disabilities. The bottom line is that this method works in real life situations.

#### **4. Conclusion**

Cognitive ERPs are capable of monitoring a wide variety of cognitive processes in a reliable and valid manner with or without accompanying behavioral responding. They have demonstrated the ability to serve clinical assessment, monitor therapeutic progress, and assist in prognosis. In fact, ERPs can provide information in situations where no other method can, such as with patients experiencing severe communication and motor impairments. They can also serve as adjunctive methods in situations that permit traditional assessment as they provide a unique level of information capable of informing the clinician of problems where traditional tests do not (as seen with the LG case study above). While neu-

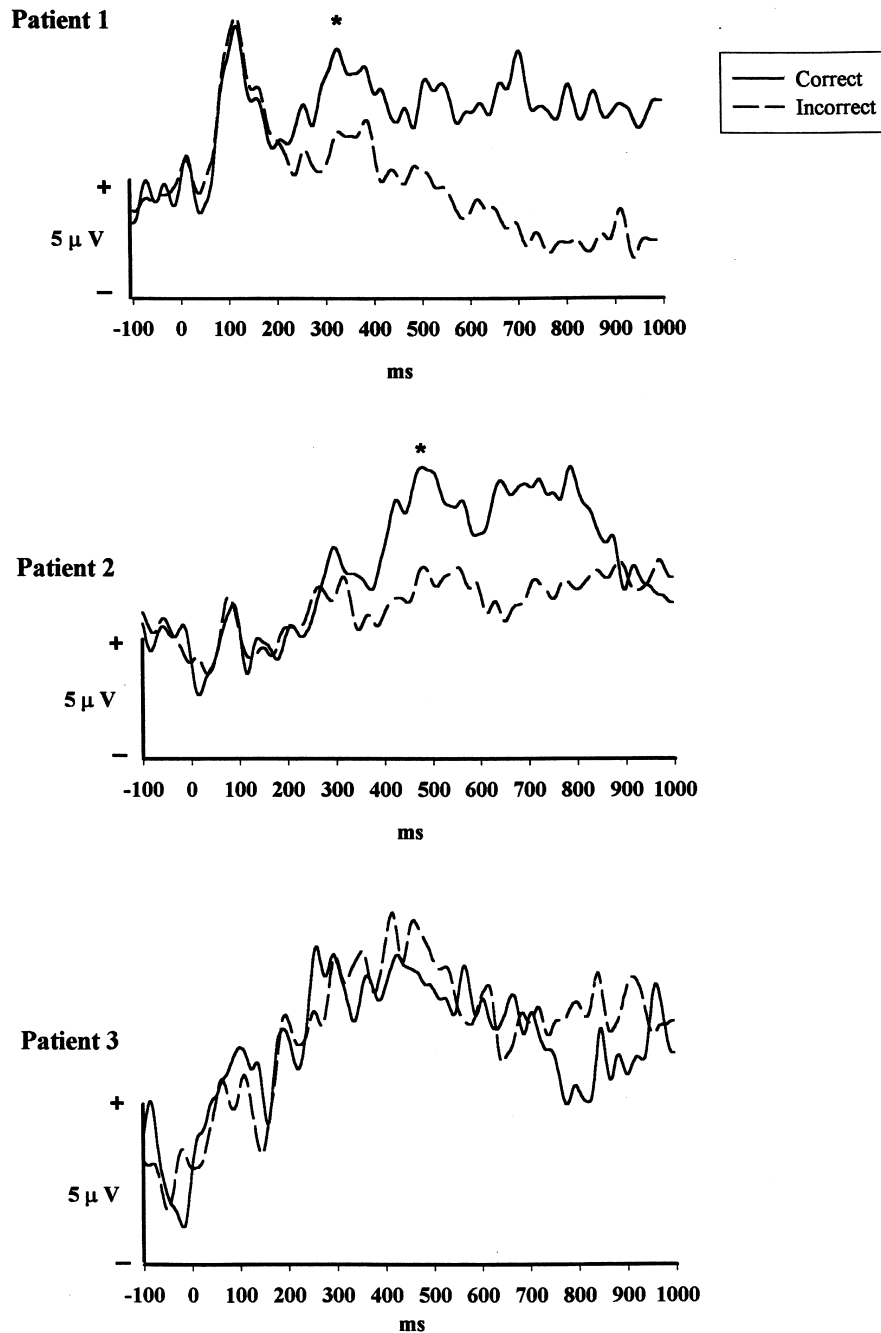


Fig. 5. Individual ERPs obtained on the PALPA from three stroke patients (Pz). Patients 1 and 2 both showed significantly larger P300 responses (asterisk) to correct pictures than to incorrect pictures. In contrast, patient 3 failed to show observable differentiation between conditions. All other details as in Fig. 1.

ropsychological tests may depend on a variety of cognitive processes, they are generally partitioned

on the basis of the major function(s) they purport to measure. The behavioral measurements ob-

tained from these tests are limited in their ability to delineate these underlying cognitive processes. The use of ancillary ERP methods provide an on-line index of the cognitive processes involved in a particular task and are paramount to determining the individual strategies used.

Techniques such as those encompassed in the Innovative Assessment Methods Program represent an essential development in clinical monitoring particularly when health care systems in many regions are under financial pressure. It is also a situation that will steadily worsen as baby boomers reach ages of increasing risk for stroke and Alzheimer's disease, for example. Many therapeutic interventions (e.g. various rehabilitation procedures) involving neurological insult cases carry with them extended costs due to extended therapy periods and intensive personnel involvement. There is an understandable reluctance to commit resources to patients who may not be able to benefit from certain procedures. In most situations, patients who are incapable of communication and, therefore, who are incapable of being assessed, fall, by default, into that category of patients who are judged to show no signs of benefiting from therapeutic intervention. This is a situation experienced by a variety of patient groups from cerebral palsy (Byrne et al., 1995a) to traumatic brain injury (Connolly et al., 1999b). The latter case study is particularly germane and merits a brief description to emphasize the impact the techniques described above can have on a patient's future.

HF was a 21-year-old man who suffered a traumatic brain injury as a result of being stabbed through the head with a knife. Having survived the attack, he was admitted to a rehabilitation setting for assessment. The severity of his injuries rendered him globally aphasic and physically impaired to a level that prevented him from making reliable movements of any type. Traditional assessment could not be conducted and rehabilitation was not recommended as he appeared to have no apparent cognitive functioning abilities. He was referred for ERP testing and was found to have intact speech comprehension abilities despite being unresponsive to all verbal challenges. On the basis of these ERP findings, he was admit-

ted to a rehabilitation program that culminated in an excellent outcome. Without such intervention, this patient would have failed to return to a productive life, presuming he survived at all.

Research over the last 35 years has demonstrated the sensitivity of ERPs to a plethora of cognitive functions and current research is extending these boundaries continuously. The time has arrived to apply this extensive knowledge base to those individuals experiencing cognitive problems due to various neurological insults including stroke, traumatic brain injury, and neurodegenerative disorders. The research encompassed in the Innovative Assessment Methods Program aims to do precisely that.

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