How Does Severity of Aphasia Influence Individual Responsiveness to Rehabilitation? Using Big Data to Understand Theories of Aphasia Rehabilitation

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ABSTRACT

Our ability to make great progress in delivering, optimizing, and predicting rehabilitation outcomes for individuals with aphasia is challenged by factors that influence rehabilitation outcomes. These include patient demographic factors such as age, education, and neurologic factors such as time poststroke, the site and size of the lesion, and the resulting severity of language impairment. Also variable across individuals is the type of treatment and its duration and intensity. This article examines the utility of big data analysis for understanding one of these factors, severity of impairment, and how individual responsiveness to rehabilitation is influenced by a patient’s severity of language and cognitive impairment(s). Using examples from two studies and a larger data set, we show that when rehabilitation is tailored to an individual’s specific level of impairment, severe and mild patients both show improvements in accuracy and latency. Furthermore, more severe patients tend to show substantial gains on targeted rehabilitation tasks as well as on standardized tests. These results provide support for recent reviews of aphasia rehabilitation studies in concluding that systematic aphasia rehabilitation is indeed effective, and importantly, severity is not a negative prognostic indicator for successful outcomes.

KEYWORDS: Big data, rehabilitation, technology, aphasia, individual responsiveness
Learning Outcomes: As a result of this activity, the reader will be able to (1) describe the various factors that influence rehabilitation outcomes and studies that have examined these factors and (2) identify how large data sets can help deconstruct the influence of severity of language impairment on rehabilitation outcomes in aphasia.

One of the most important goals of rehabilitation of aphasia is to enable patients to achieve functional communication independence. Therefore, clinicians’ goals are to provide patients with the individualized treatment programs that are likely to work, taking into account their individual characteristic and demographic profile. A first step is to understand the basic principles of neuroplasticity that likely influence rehabilitation outcomes. Animal models help us to understand these principles.1,2 For instance, we know that learning and experience results in plasticity even in the adult brain. After brain damage, cortical plasticity depends on the undamaged tissue in the damaged hemisphere and, most importantly, more intensive training increases plasticity.2 Recent advances in neuroimaging have also provided some understanding of the neurologic factors that predict the degree of language impairment3,4; however, to what degree this impairment can be modified with rehabilitation is unknown.

It is also not clear how much therapy is enough for individual patients in terms of dosage and intensity. Consequently, research in aphasia rehabilitation is not yet at a point to be able to predict the degree of improvement for individual patients after rehabilitation. One reason for this problem is that no two patients are alike in their manifestations of aphasia and there are a host of factors that influence impairment and outcomes. These include factors such as age, education, as well as time post-stroke, the site and size of the lesion, and the resulting severity of language impairment.5,6 The type of treatment provided, as well as its duration and intensity, also is varied across studies.

Interactions among these variable factors make it difficult to evaluate the effect of rehabilitation on improving communication skills. Therefore, it is not surprising that recent reviews of treatment effectiveness have had mixed outcomes. For instance, some recent meta-analyses have argued for the beneficial effect of rehabilitation in chronic stroke survivors7,8; others, including a Cochrane review of randomized control trials in aphasia have been less favorable.9 A recent influential study suggested that rehabilitation was no more effective in promoting change on the measured outcomes than everyday communication with hospital volunteers in acute stroke survivors.10 In the Cochrane review of randomized control trials, several studies have included large samples of patients, but the results have not been particularly encouraging largely because of the interactions between factors such as severity, type of treatment, and intensity.

Some studies suggest that more intensive treatment results in better outcomes in both chronic and in acute patients with aphasia11–14; other studies, including a randomized controlled trial have found that intensive treatment (up to 5 hours per week) was no better than standard treatment (1 to 2 hours per week).15 Therefore, it is currently difficult to draw conclusions about whether more intensive rehabilitation is indeed effective and what the optimal intensity, duration, or approach of treatment for individual patients may be.

On the other hand, studies that have examined the efficacy of specific treatments on individual patients using single subject experimental design and/or case series designs have been able to systematically and successfully demonstrate when and why certain treatments work and do not work.16 The goal of such carefully controlled treatment studies is to then scale successful treatments to a larger heterogeneous population so that the role of factors such as age, severity of impairment, and intensity of treatment can be delineated. Potentially, with large scale studies of aphasia, we can begin to stratify patients into smaller cohorts of similar patients to then examine the various factors that influence therapy outcomes, such as age, lesion location, education, severity of impairment, and type of treatment among other things.
The increasing use of technology in service delivery is beginning to make such examinations possible. A major advantage of recent technological innovations in health care is that it makes it possible to collect data remotely, thereby alleviating the practical difficulties of requiring every patient to come to an actual physical setting to receive therapy. Computer programs also provide an opportunity for patients to practice more intensely and consistently than what is typical in weekly/biweekly visits to a clinical location. This, in turn, makes it possible to examine the influence of treatment intensity on rehabilitation outcomes.

Recent studies have examined the efficacy of rehabilitation techniques, such as videoconferencing for individuals with brain injury and Skype-delivered therapy for individuals with aphasia. Still other studies have developed virtual speech therapists; such software programs are capable of delivering scripted therapy to patients while providing appropriate feedback based on the patients' responses. Finally, there are several software programs that provide self-paced, cued treatments. Of these, the Multicue software makes different types of cues (semantic, phonemic, general information) available to patients as they practice word retrieval. Results from 18 patients with aphasia who received Multicue therapy improved on the Boston Naming Test (BNT), but the changes were not significant when compared with the control group. A similar program, MossTalk, also provides patient-initiated cues during word retrieval. This program was shown to be effective in increasing patients' comprehension and lessening word-retrieval deficits in aphasic individuals and those who had semantic dementia. Using a software called StepByStep, Palmer et al found the 15 patients assigned to a computer treatment group showed more improvement on their naming ability than did 13 patients who practiced everyday language activities, including conversation and support groups and reading and writing activities. Our previously described software program, Constant Therapy (Constant Therapy, Inc., Newton, MA) can provide a range of language and cognitive rehabilitation tasks for individuals with stroke and traumatic brain injury. This program allows patients to receive impairment-focused treatment that is targeted toward their specific language or cognitive impairments.

In this article, we illustrate the utility of big data in understanding some long-standing and elusive questions about the effectiveness and optimization of rehabilitation outcomes. We focus here on one factor, severity of aphasia, which is likely to influence individual responsiveness. Like most other such factors, the evidence for severity to influence outcomes is mixed. In patients with acute aphasia, one randomized control trial showed that patients with mild aphasia improved more than patients with severe aphasia. Another study showed that even severe patients with aphasia benefited from very early language therapy. However, Pedersen and colleagues showed that initial aphasia severity predicted language impairment in the chronic stage and was associated with poorer outcomes in the long term. In general, the evidence is mixed about whether patients who are more severely impaired make more or fewer gains after rehabilitation. One large-scale study examined overall stroke outcomes (not specifically language) and found that greater severity predicted a poorer outcome after rehabilitation. In contrast, in one meta-analysis, Robey showed that acute patients with severe aphasia show substantial gains after treatment but chronic patients with moderate and severe aphasia also show substantial gains after rehabilitation. Likewise, Persad and colleagues reviewed outcomes from rehabilitation centers that provide intensive comprehensive aphasia treatment and found both mild and severe chronic patients with aphasia to benefit from such treatment.

To summarize, more work needs to be done to systematically examine the influence of severity on language rehabilitation outcomes in patients with aphasia. Inherent in the mixed outcome is the variability of rehabilitation approaches that have been implemented to improve language outcomes. In this article, we describe rehabilitation data obtained from a standardized rehabilitation program that provides the same type of impairment-based therapy to a heterogeneous group of patients but is tailored to each individual patient's specific language and cognitive impairment.
we illustrate how large data sets allow us to examine the role of severity in accounting for patients’ individual responsiveness to rehabilitation. In this previously published study, we reported changes in quantitative data such as accuracy and latency on specific treatment tasks. In study 2, we illustrate how such data sets may also be examined to understand the way in which individual patients engage with therapy with regard to self-cueing. This provides a qualitative view into how severity of impairment interacts with patients who use differing amounts of assistance. Finally, in a third example, we provide some preliminary insights on the influence of severity from an even larger data set consisting of over 1,000 patients.

STUDY 1: INDIVIDUAL RESPONSIVENESS TO THERAPY BASED ON PATIENT SEVERITY

In a previous study, the effect of an individualized treatment program on rehabilitation outcomes was examined. Fifty-one individuals with language and cognitive deficits were administered standardized tests (Revised Western Aphasia Battery [R-WAB], Boston Naming Test [BNT], Pyramids and Palm Trees [PAPT], and Cognitive Linguistic Quick Test [CLQT]) before and after completion of therapy. The individual R-WAB Aphasia Quotient (AQ) and CLQT composite severity varied along a continuum of severity. All participants suffered either a stroke or a traumatic brain injury, ranging from 1 to 359 months postonset (mean = 59.6, standard deviation = 69.5) months postonset. Participants ranged in age from 38 to 87 years (mean = 64.2, standard deviation = 10.7). Forty-two experimental patients used the Constant Therapy software application on the iPad Apple Inc, Cupertino, CA once a week with the clinician and up to 6 days a week for home practice. Nine control patients practiced Constant Therapy on the iPad once per week with the clinician only. Thirty-eight therapy tasks were divided into language and cognitive activities. During the first session, the clinician assigned a series of tasks as baseline. A given task was assigned to treatment as long as baseline accuracy on that task was less than 80%. Once a set of tasks were assigned, the patient practiced them with the clinician on a weekly basis. The experimental patients practiced in the clinic and at home; control patients practiced in the clinic only. Each task was practiced until accuracy on that task reached at least 95% on multiple occasions. At that point that task was replaced with the task at the next level of difficulty.

All 51 patients completed a 10-week program leading to total of 3,327 therapy sessions across patients. Initial linear mixed model analysis showed that both the experimental and control groups improved, but experimental participants improved on significantly more therapy tasks that they were assigned relative to control patients. Also, although both groups benefited from this therapy program, the experimental group showed more improvement than the control group on standardized tests. Thus, more practice with the therapy tasks appeared to result in greater changes.

A further analysis examining the relationship between severity of language/cognitive impairment and treatment outcomes was also performed. The analysis stratified patients according to whether they scored lower or higher than the average on the R-WAB AQ or CLQT composite score and a linear mixed effect analysis was then conducted. A positive effect of R-WAB AQ or CLQT composite severity scores indicated that participants with higher than average severity scores showed more improvement on the task. Likewise, a negative effect of R-WAB AQ or CLQT composite severity scores indicated that participants with lower than average severity scores showed more improvement on the task. Four interesting patterns of results thus emerged. Patients with lower than average R-WAB AQ scores tended to benefit from tasks such as sound to letter matching and word identification, suggesting that more severe impaired patients tended to benefit from some of the simpler language tasks. Patients with lower than average CLQT composite severity scores also tended to benefit from tasks such as category matching and picture matching, indicating again that patients with more severe cognitive impairment benefited from tasks that targeted short-term memory. In contrast, patients with higher than average R-WAB AQ scores
showed improvements in tasks such as picture matching, indicating that for patients with higher language skills, a task that engaged language and short-term memory was beneficial. Likewise, patients with higher than average CLQT composite scores tended to benefit from tasks such as map reading, which also rely on both language and cognitive processing abilities. Similar findings were obtained for changes in latency. The results also showed that patients with more severe language impairment and less severe cognitive impairment gained in accuracy on tasks relying on good cognitive skills but that required less language processing (e.g., map reading); patients with more severe cognitive impairment and less severe language impairment showed gains in processing speed on tasks such as picture matching. Collectively, these results suggest an interaction between language and cognitive processing during language rehabilitation. Although this is not a surprising finding, it does underscore the need for clinicians to be aware that rehabilitation tasks can target language and cognitive processing depending on the individual patient needs. Also, these results show that individual patient language and cognitive impairment severity can determine the degree to which they benefit from specific rehabilitation tasks.

When examining changes on standardized tests as a function of rehabilitation, more severe patients (i.e., patients with lower R-WAB AQ scores) showed greater changes on R-WAB AQ and PAPT after rehabilitation than less severe patients. Lower CLQT scores were negatively correlated with changes on R-WAB AQ, several subtests of the CLQT (attention, executive functions, language, visuospatial skills, and composite severity), and changes in their PAPT scores due to therapy. This indicated that patients who had lower cognitive scores showed greater changes than less severe patients on these measures. Finally, these results indicate that patients with more severe language and cognitive impairments can show consistent and robust gains on therapy tasks and standardized tests, in the latter case, surpassing the gains made by less severe patients. These findings are consistent with the meta-analysis of various language rehabilitation studies, where Robey suggests that given the extent of impairment, moderately and severely impaired patients can make substantial improvements, presumably with the appropriate rehabilitation.

The results of this study illustrate the influence of severity of impairment on rehabilitation outcomes in terms of changes in accuracy and latency. However, examining systematic session-by-session performance on a variety of language and cognitive rehabilitation tasks also permits the examination of the influence of individual differences in severity on qualitative outcomes after rehabilitation. The study described next examines how individual patients seek and obtain assistance to complete rehabilitation tasks and how this self-administered cueing is influenced by severity of language impairment des Roches et al, (in preparation). Examining the nature of self-administered hints and/or cues in computer-based treatments are a unique feature of these computer programs. Programs such as Multicue and Mos Talk (described earlier) also allow patients to request and obtain cues to complete the word retrieval task. In the study described next, the types of cues that patients can chose to obtain to complete tasks vary depending on the task, we, therefore, prefer to refer to them as “self-administered hints” rather than cues.

**STUDY 2: INDIVIDUAL RESPONSIVENESS TO SCAFFOLDING DURING INTERVENTION**

The 51 individuals who were studied using the Constant Therapy software application over the 10-week therapy program were allowed to use hints specific to each task. Twenty-eight of the 37 tasks included buttons that revealed a hint to answering the item. Hints included repeating the task instructions, repeating the audio stimulus for tasks that had audio presentations, or repeating additional audio stimuli (such as the sound of the letter) provided within the task. Hints were chosen by the participants who could use them as often as they chose. The Constant Therapy software generated reports for each participant. This report included the average accuracy for every session.
and a total number of hints used in each session, for each level, for all tasks that were completed by the participant.

Only tasks that provided hints and that patients completed three or more times were considered. Consequently, across the 51 patients and 28 different tasks that provided cues, 13,668 tokens of data were available for analysis, as follows. First, to examine the relationship between hint use and accuracy by patients, a simple linear regression was run for each of the 51 patients to see if hint use predicted accuracy on the tasks where hints were used. Twenty-four patients (47.1%) produced significant regression equations, in each case, the slope coefficients indicated the direction of the relationship between hint use and accuracy. To understand more about the direction of the relationship between hint use and task accuracy, a K-means cluster analyses were completed for all patients to examine if these different patterns of relationship between hint use and accuracy was systematic across patients. Results from the cluster analyses showed that all patients fit into one of five profiles (see Fig. 1):

1. An increase in accuracy with greater hint use (“upward profile,” \( n = 13 \))
2. A curvilinear trend with an initial increase in accuracy with greater hint use (“curvilinear, initial upward profile,” \( n = 9 \))
3. A curvilinear trend with an initial decrease in accuracy with greater hint use (“curvilinear, initial downward profile,” \( n = 11 \))
4. A decrease in accuracy with greater hint use (“downward profile,” \( n = 14 \))
5. No hint use (\( n = 4 \))

What factors determined why participants used hints? To answer this question, the frequency of hint use was correlated with scores on R-WAB, CLQT, BNT, PAPT, and American Speech Language Hearing Association Functional Assessment of Communication Skills (ASHA FACS)\(^{45}\). All correlations and were negative and significant (ranging between \(-0.475\) to \(-0.641\) for R-WAB AQ and ASHA FACS respectively, \( p < 0.001 \)). This finding indicated that patients who had more severe aphasias tended to utilize more hints throughout the rehabilitation program.

We next examined whether severity of language and cognitive impairment determined the frequency of hint use and whether it was ultimately beneficial or not. Some interesting patterns emerged. A multivariate analysis of variance indicated that the upward, downward, and little/no-hint-use patient cluster profiles differed in their frequency of hint use, R-WAB, AQ, CLQT composite score, BNT score, and ASHA FACS communication index scores. As can be seen in Fig. 2, patients who had little/no hint use (gray line, Fig. 2) used hints

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**Figure 1** Number of participants in each of the five profiles of patients’ relationship between hints use and accuracy on tasks. The colored bars represent participants who had displayed specific profiles of relationships whereas the gray bar indicates the number of patients who did not use any hints.
infrequently and had higher scores on most of the standardized tests than did other patients. Next, patients in the “upward” profile cluster used hints less frequently but their use was associated with higher accuracy (dark green, Fig. 2); these patients had the second highest standardized language, cognitive, and communication scores. Notably, patients in the “downward” profile cluster used hints most frequently but this higher hint use was associated with lower accuracy, and therefore, not beneficial for them (dark red, Fig. 2). These individuals had the lowest R-WAB AQ, CLQT composite, BNT, and ASHA FACS communication index scores.

These results indicate that the more severe patients used hints more frequently, but this higher hint use was not beneficial. Similarly, the less severe patients used hints less frequently, but this hint use was beneficial. These results have implications for the way self-administered hints or clinician-generated cues may help or hinder patients during rehabilitation. Given the typical abundance of clinician-provided cues during language therapy and its extension into self-administered cues in computer-based language therapy programs, it is important consider its potential benefits and downsides. Clearly, not all patients benefit from hints or cues to the same extent. These preliminary findings indicate that the more severe the patient the more reliant he/she may be on cues, but the less beneficial it may be for that individual. One simple clinical solution to this...
apparent differential utility of cueing might be to assess its value informally prior to implementing a cueing strategy, as well as to ask the patient whether or not it is of help. When discrepancies exist between the assumed and the demonstrated value of hints, this should be made clear to the person with aphasia. This could be built into computerized rehabilitation as well.

**FUTURE DIRECTIONS WITH VERY LARGE DATA SETS**

Although the work described previously illustrates how moderately large data sets can begin to inform clinicians and researchers about how individual patients respond to rehabilitation, even larger data sets can help further our understanding of how rehabilitation works for large groups of patients. This still permits researchers to continue to examine individual differences in what helps or is ineffective for individual patients. In this type of analysis, several hundred patients perform a given task as users of the Constant Therapy platform. It should be noted that this is not a typical research study as the data comes from users paying for this service. However, the large amounts of anonymized data collected during this process allows careful examinations of what treatments work as well as the extent of improvements individual patients show on treatment tasks.

As an example of how such data can be analyzed and interpreted, data from a total of 465 patients who suffered from chronic post-stroke aphasia was examined. These patients downloaded the app on their iPads/tablets and created a Constant Therapy account. As in the Des Roches et al study, a given task was assigned as long as performance on the task was between 40 and 90% accuracy and (less than 80th percentile in latency). Therefore, patients could be assigned one or more of the 56 tasks that also varied by different levels of difficulty. For a given task type and level, the average of the last 10 items for each patient was compared with the average of the first 10 items for each patient for all the individuals who performed that specific task using a paired t-test. Because it takes a few trials for each individual to understand how to do a specific task, the first three items of a given task were dropped from the analysis. What results is an extensive listing of all therapy tasks and levels that show a significant change at the end of rehabilitation relative to the beginning of rehabilitation and are depicted in Fig. 3. This figure provides an overall snapshot of the effectiveness of treatment but it does not really provide specific information about which therapy tasks work for which types of patients.

To more completely understand the influence of severity on improvements on rehabilitation, we can further filter the information based on starting severity of impairment. As an example, let us take one specific task, following auditory commands (level 2). In this task, patients are asked to place pictures in a grid based on specific auditory instructions by following two-step commands (e.g., place the box to the right of the pen and then place the brush below the box). As can be seen in Fig. 4A, when the entire set of 402 patients whose initial performance was less than 90% accuracy was examined, the average accuracy gain in points was 10.73. When filtered to patients whose initial performance is less than 80% accuracy, the average accuracy gain is 15.14 and to patients who show less than 70% accuracy at initial performance, the average accuracy gain in points was 18.88. When filtered to patients who show less than 60% accuracy at initial performance, average accuracy gain in points was 23.56, and when filtered to patients who show less than 40% accuracy at initial performance, average accuracy gain in points was 32.65. Thus, when the data were filtered to reveal the results of more severely impaired patients (lower accuracy at initial performance), they show that these patients make larger accuracy gain in points (see Fig. 4A). A similar effect is observed for another therapy task, sound identification, which requires phonological segmentation (e.g., does this word contain the sound /puh/?). As Fig. 4B shows, patients with 60 to 40% initial accuracy show accuracy gains ranging between 23 and 45 points. These results begin to highlight how it is possible to stratify the patient outcomes in terms of their initial severity at the beginning of therapy.
The main finding from such analyses is that all patients show strong gains after this treatment, but more severe patients show even stronger gains. This lends further support for studies that have highlighted the importance of systematic treatment for patients with aphasia and shows that when treatments are targeted at the individual’s specific impairment, optimal gains can be expected. Ultimately, such data can also help to predict the amount of gains that can be expected for individual patients. For instance, if it is known that patients with moderate to severe auditory comprehension deficits with baseline accuracy of 40% can expect to see an average gain of 32 points, this information can be used to set the expectations for individual patients who have similar profiles.

**DISCUSSION**

This article provided some examples of how large-scale data sets can inform our understanding of rehabilitation in aphasia. Using the example of one of the factors that influences aphasia impairment and outcomes, for example, severity of impairment, we illustrated how systematic evaluation of severity results in a clearer understanding of how patients with moderate to severe language and cognitive deficits respond to treatment differently than patients with milder language and cognitive deficits. The main observations are as follows: (1) study 1 showed that patients with more severe language impairment and less severe cognitive impairment showed more gains on standardized tests of language and cognition than less severely impaired patients; (2) study 1 also showed that patients with more severe language and cognitive impairments tended to rely on self-administered cues more often but these cues were not necessarily beneficial or successful in performing the tasks accurately. In contrast, patients with less severe language and cognitive impairments rarely used cues but when they did, the cues appeared to help...
with succeeding at the task; and (4) analysis of a larger data set showed that patients with moderate to severe aphasia showed substantial gains on therapy tasks that were targeted at their impairment. These findings are consistent with other studies that suggest that patients with more severe language and cognitive deficits have more to gain from treatment, and when provided with the appropriate treatment, can indeed make such gains.38,39

Figure 4  (A) Average gain in accuracy in points (primary y-axis) plotted against the number of patients (secondary y-axis) for bins of patients filtered by starting level performance as a proxy for severity, shown on the x-axis. Performance is shown for the auditory command task level 2, which involves following two-step commands. (B) Average gain in accuracy in points (primary y-axis) plotted against the number of patients (secondary y-axis) for bins of patients filtered by starting level performance as a proxy for severity, shown on the x-axis. Performance is shown for the sound identification task that requires phonological processing.
Using big data is not the only solution or the primary approach to understanding the effects of rehabilitation in poststroke aphasia. There are several limitations with collecting such types of big data because large data sets tend to be anonymized and preclude systematic examinations of important personal demographic information. There are other factors that naturally allow themselves to be analyzed with big data such as intensity, frequency, and duration of therapy practice because software programs can systematically log the duration of treatment, the number of items practiced, and frequency of practice. Therefore, these big data sets can begin to answer questions about factors that influence rehabilitation outcomes but may not provide the confirmatory answers for optimal rehabilitation for individual patients. Also, big data mining should be viewed as a tool to help understand critical questions concerning rehabilitation of aphasia. Therefore, this tool is only as good as the questions that are asked about rehabilitation and the hypotheses that we seek to confirm or disconfirm.

To conclude, the results presented in this article support recent reviews of rehabilitation studies in aphasia that conclude that systematic aphasia rehabilitation is indeed effective and severity does not have to be a negative prognostic indicator for successful outcomes.

DISCLOSURE
Swathi Kiran has a significant financial interest in Constant Therapy, she is a cofounder and a scientific advisor for the software company. This article does not describe the software per se, but discusses the data and interpretation of results obtained from studies using the software program.

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