Triangulation of language-cognitive impairments, naming errors and their neural bases post-stroke

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ABSTRACT

In order to gain a better understanding of aphasia one must consider the complex combinations of language impairments along with the pattern of paraphasias. Despite the fact that both deficits and paraphasias feature in diagnostic criteria, most research has focused only on the lesion correlates of language deficits, with minimal attention on the pattern of patients' paraphasias. In this study, we used a data-driven approach (principal component analysis - PCA) to fuse patient impairments and their pattern of errors into one unified model of chronic post-stroke aphasia. This model was subsequently mapped onto the patients' lesion profiles to generate the triangulation of language-cognitive impairments, naming errors and their neural correlates. Specifically, we established the pattern of co-occurrence between fifteen error types, which avoids focussing on a subset of errors or the use of experimenter-derived methods to combine across error types. We obtained five principal components underlying the patients' errors: omission errors; semantically-related responses; phonologically-related responses; dysfluent responses; and a combination of circumlocutions with mixed errors. In the second step, we aligned these paraphasia-related principal components with the patients' performance on a detailed language and cognitive assessment battery, utilising an additional PCA. This omnibus PCA revealed seven unique fused impairment-paraphasia factors: output phonology; semantics; phonological working memory; speech quanta; executive-cognitive skill; phonological (input) discrimination; and the production of circumlocution errors. In doing so we were able to resolve the complex relationships between error types and impairments. Some are relatively straightforward: circumlocution errors formed their own independent factor; there was a one-to-one mapping for phonological errors with expressive phonological abilities and for dysfluent errors with speech fluency. In contrast, omission-type errors loaded across both semantic and phonological working memory factors, whilst semantically-related errors had the most complex relationship by loading across four factors (phonological ability, speech quanta, executive-cognitive skills and circumlocution-type errors). Three components had unique lesion correlates: phonological working memory with the primary auditory region; semantics with the anterior temporal region; and fluency with the pre-central gyrus, converging with existing literature. In conclusion, the data-driven approach allowed derivation of the triangulation of deficits, error types and lesion correlates in post-stroke aphasia.

1. Introduction

The most common cause of aphasia is stroke, with approximately 30% of cases suffering from language problems in the acute phase and 20% chronically (Berthier, 2005; Engelter et al., 2006). Clinical diagnosis and management of aphasia is founded on establishing the pattern of language deficits and preserved skills. In addition, perhaps more than in any other disorder of higher cognition, aphasiology also heavily emphasises the types of speech errors made by patients, with both deficits and paraphasias featuring in diagnostic criteria. In recent years,

considerable advances in knowledge and analysis techniques have been made by large-scale studies that have mapped language deficits and the underlying principal computational components to the patients' lesion distributions (e.g. Bates et al., 2003; Butler et al., 2014; Corbetta et al., 2015; Halai et al., 2017; Lacey et al., 2017; Mirman et al., 2015a; Mirman et al., 2015b). Given their importance in aphasiology, the key purpose of the current study was to assimilate the patterns of patients' paraphasias thereby generating the much broader lesion-symptom-error mapping for post-stroke aphasia, for the first time.

In order to resolve the triangulation of lesions, symptoms and error

types, each of the pairwise combinations is required. For the link between language impairments and error types, we might start with the most straightforward hypothesis that there is a one-to-one mapping (for example, phonological impairments with phonological paraphasias). Studies of individual error types or specific patient groups, however, have shown that this simple hypothesis is incorrect. For example, seminal studies of semantic errors (cf. Morton and Patterson, 1980) noted that these could arise from multiple different underlying impairments, and conversely most patients generate a collection of different paraphasias (Schwartz et al., 2006). Whilst a variety of paraphasias can reflect multiple co-occurring deficits in each patient, multiple error types are generated even in disorders such as semantic dementia (omissions, superordinate and coordinate semantic errors, and partial descriptions: Lambon Ralph et al., 2001; Woollams et al., 2008), which is characterised by a selective semantic impairment and atrophy consistently centred on the anterior temporal region (Mummery et al., 2000; Warrington, 1975). Taken together, these results suggest that (i) different error types can co-occur because they are generated by the same underlying impairment and also (ii) that the same error type can be caused by more than one type of deficit. In order to unpick the 'many-to-many' relationships between error types and impairments in post-stroke aphasia, we utilised principal component analysis with varimax rotation on a large patient dataset in order to extract: (a) how different error types cluster and differentiate across patients; and (b) the underlying principal ways in which impairments and error types co-occur and dissociate.

In comparison to the relative paucity of aphasiological studies linking error types and impairment patterns, there have been many explorations of the relationship between different language impairments and their associated lesions, over the long history of aphasiology. In addition, this mass of research activity continues to spawn ever more sophisticated methods to relate impairments and lesions (e.g., lesion mapping: (Damasio and Damasio, 1980); voxel-based lesion-symptom mapping: (Bates et al., 2003); multivariate symptom decomposition: (Lambon Ralph et al., 2003); and multivariate lesion mapping: (i.e. Hope et al., 2013; Yourganov et al., 2015; Zhang et al., 2014). Numerous studies have conducted voxel-lesion mapping for individual language tasks (e.g., repetition, naming, comprehension, etc. (i.e. Baldo et al., 2013; Baldo et al., 2012; Dronkers et al., 2004) or features of aphasic performance (e.g., fluency: Borovsky et al., 2007). Extracting an exact understanding of the cognitive and neural bases for aphasic performance, from such analyses, is challenging for a number of reasons. First, any given cognitive-language task relies on multiple different processes/computations (e.g., naming requires visual decoding, semantic activation, phonological processing and articulation) and thus poor performance on the same task can arise for different reasons, each with different neural bases. Secondly, patients with more severe deficits perform poorly across many different tasks, albeit potentially for different reasons. This is because, thirdly, lesions correspond to the vascular rather than functional structure, and thus infarcts often disrupt multiple processes. In order to isolate the key cognitive dimensions underlying aphasic performance and their associated neural substrates, we recently applied principal component analysis (PCA) with varimax rotation on a substantial and detailed behavioural dataset to yield cognitively-interpretable, statistically-independent factors, which are ideal for use in voxel-based lesion-symptom mapping (Butler et al., 2014; Halai et al., 2017). Accordingly, in the current study we utilised the same approach on a larger patient database containing both performance across a detailed neuropsychological battery and coding of all the naming errors generated by the same patients.

With regard to the final part of the triangulation, error-lesion mapping, again, there is a relatively limited number of studies in the current literature. Few, if any, studies have tackled all aphasic paraphasias simultaneously. Instead, a handful of previous studies have focussed on two of the most prominent error types: semantic and phonological errors. In a series of studies of chronic aphasia, Schwartz

and colleagues found that semantic errors were associated with damage to the left anterior temporal lobe (ATL), prefrontal and posterior temporal areas though these two non-ATL correlates disappeared when performance variance on an executively-demanding semantic task was partialled out (Schwartz et al., 2012; Schwartz et al., 2009; Walker et al., 2011). In contrast, Cloutman et al. (2009) found an association between semantic errors and hypoperfusion of the left posterior temporal lobe (BA 37) in acute stroke cases, though it is hard to compare these studies directly as they varied: (i) in the types of patient included, (ii) the definition of error types, (iii) the measure of brain integrity (lesion vs. perfusion), and (iv) the formal of analysis (including covariates). There was much greater consistency across these studies, however, with regard to phonological errors, which were associated with damage to precentral gyrus (preCG: (Cloutman et al., 2009; Schwartz et al., 2012; Walker et al., 2011). Although aphasic patients generate many other types of paraphasia beyond semantic and phonological errors, few have explored their neural correlates and their relationship to the patients' impairments (for two important exceptions that explored semantic and phonological errors alongside background neuropsychological results, see Mirman et al., 2015a; Mirman et al., 2015b). This includes omission errors which, although very common, are often discarded from analyses (because this error type, by itself, provides no clues as to its source). To address these challenges in the present study, we (a) included all paraphasia types; (b) used a data-driven approach to cluster co-occurring error types (rather than using a user-defined set of criteria for collapsing errors); and explored the relationship of the grouped paraphasias to the patients' pattern of impairments and the lesion correlates.

2. Materials and methods

2.1. Participants

Fifty-one chronic stroke patients (either ischaemic or haemorrhagic) were recruited into the current study, who had impairment in producing and/or understanding spoken language. No restrictions were placed according to aphasia type or severity (spanning global to minimal aphasia). Given the emphasis on a full range of error types, in this study we excluded five patients who did not attempt at least 50% of items in each naming test. All patients were at least 12 months post-stroke at the time of scanning and assessment, were native English speakers with normal or corrected-to-normal hearing and vision (see Supplementary Table 1 for demographic details). In brief, there were 33 males and 13 females with a mean age of 65.46 years (SD = 11.49). The mean years of education were 12.07 years (SD = 1.97) and mean months post-stroke were 54.65 (SD = 43.28). Participants were premorbidly right-handed, had one stroke and did not have any other significant neurological conditions. Informed consent was obtained from all participants prior to participation under approval from the local NHS ethics committee. MRI data from a healthy age and education matched control group (8 female, 11 male) was used in the lesion identification procedure for each patient (Seghier et al., 2008).

2.2. Neuropsychological assessments and analysis

Explicit naming responses to the 64-item naming test from the Cambridge Semantic Battery (CNT) (Bozeat et al., 2000) and 60-item Boston Naming Test (BNT) (Kaplan et al., 1983) were recorded and coded for error type. The CNT contains 64 items (spanning three living and non-living categories: animals, bids, fruits, household items, tools and vehicles). The BNT is relatively harder as it is graded in difficulty; it consists of 60 black and white line drawings. In both cases, the patient was shown each item and asked to provide the name. The first complete (i.e., non-fragment) response for each item was scored. Fragmented responses were taken into account in the case of initial phoneme errors (INITIAL) where a fragmented response was given without any further