Artificial grammar learning in vascular and progressive non-fluent aphasias

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ARTICLE INFO

ABSTRACT

Patients with non-fluent aphasias display impairments of expressive and receptive grammar. This has been attributed to deficits in processing configurational and hierarchical sequencing relationships. This hypothesis had not been formally tested. It was also controversial whether impairments are specific to language, or reflect domain general deficits in processing structured auditory sequences.

Here we used an artificial grammar learning paradigm to compare the abilities of controls to participants with agrammatic aphasia of two different aetiologies: stroke and frontotemporal dementia.

Ten patients with non-fluent variant primary progressive aphasia (nfvPPA), 12 with non-fluent aphasia due to stroke, and 11 controls implicitly learned a novel mixed-complexity artificial grammar designed to assess processing of increasingly complex sequencing relationships. We compared response profiles for otherwise identical sequences of speech tokens (nonsense words) and tone sweeps.

In all three groups the ability to detect grammatical violations varied with sequence complexity, with performance improving over time and being better for adjacent than non-adjacent relationships. Patients performed less well than controls overall, and this was related more strongly to aphasia severity than to aetiology. All groups improved with practice and performed well at a control task of detecting oddball nonwords. Crucially, group differences did not interact with sequence complexity, demonstrating that aphasic patients were not disproportionately impaired on complex structures. Hierarchical cluster analysis revealed that response patterns were very similar across all three groups, but very different between the nonsense word and tone tasks, despite identical artificial grammar structures.

Overall, we demonstrate that agrammatic aphasics of two different aetiologies are not disproportionately impaired on complex sequencing relationships, and that the learning of phonological and non-linguistic sequences occurs independently. The similarity of profiles of discriminatory abilities and rule learning across groups suggests that insights from previous studies of implicit sequence learning in vascular aphasia are likely to prove applicable in nfvPPA.

1. Introduction

Aphasia is an impairment of speech and language that often leaves other cognitive and intellectual capacities preserved. Patients with non-fluent aphasias due to frontal lobe damage exhibit significant impairments in grammar (Caramazza and Zurif, 1976; Caplan et al., 1985; Berndt et al., 1996). The grammatical impairments in comprehension and production are separable, but tend to be highly correlated (Berndt et al., 1983), suggesting that they stem from disruption of core syntactic processes rather than processes such as memory, executive function or motor function (Wilson et al., 2011). The deficits are phenomenologically similar in patients with damage due to neurodegeneration (non-fluent variant Primary Progressive Aphasia, nfvPPA) and stroke ('Broca's aphasia'), however detailed analysis of speech output has

revealed somewhat differential impairments (Patterson et al., 2006; Thompson et al., 2013). Impairments of receptive abilities have not been compared in similar detail.

Beyond these linguistic deficits, patients with aphasia also display auditory domain general processing deficits that are not specifically related to language (Caramazza and Zurif, 1976; Dominey et al., 2003; Patel et al., 2008; Christiansen et al., 2010; Goll et al., 2010; Grube et al., 2012; Geranmayeh et al., 2014b; Zimmerer et al., 2014a, 2014b; Zimmerer and Varley, 2015; Grube et al., 2016). Such studies have raised the possibility that deficits in structured sound processing may play a prominent role in language disorders, but the nature and extent of these deficits remains unclear. It also remains unclear whether impairments in aphasia are specific to the speech domain (Conway and Pisoni, 2008), or also apply to non-linguistic auditory sequences (Christiansen et al., 2010). One study identified impairments in implicit musical sequence learning in vascular aphasia (Patel et al., 2008), but direct comparisons outside of a musical framework are lacking. If artificial grammar learning tasks tap into domain general (rather than language specific) processes, one might expect rule acquisition to generalise from sequences of nonsense words to identically structured sequences of other sounds, such as tones.

It has been commonly held that grammatical impairments are specific to complex linguistic constructs such as hierarchical relationships and the passive voice (Goodman and Bates, 1997; Grodzinsky, 2000), but there is limited evidence for such dissociations (Zimmerer et al., 2014a, 2014b). By contrast, some studies suggest that the processing of adjacent relationships may be disproportionately impaired by frontal lesions involving motor association cortex (Opitz and Kotz, 2012). Recent studies examining artificial grammar learning in agrammatic aphasia secondary to stroke have focussed on linear sentential structures with varying transitional probabilities (Schuchard and Thompson, 2017). A key outstanding question, therefore, is whether agrammatic aphasia is characterised specifically by deficits for more complex linguistic structures or rather by a more global impairment in processing structured auditory sequences (Berndt, 2000).

Artificial grammar learning tasks are particularly well suited for delineating competence in structured sequence processing, as they focus on ordering relationships in the absence of other cues (e.g., semantics, phonology or pragmatics). They test learning of the rules governing the order in which stimuli occur in a sequence (Reber, 1967). Participants are typically exposed to sequences of stimuli that follow certain rules, so that the ordering relationships between the sequence elements can be learned implicitly. They are then tested with novel sequences that are either consistent with these rules or that violate them in some way, to assess learning. The implicit nature of these tasks allows the testing of a wide range of participants, including patients with aphasia. Unlike natural language tasks, it is possible to present structurally identical sequences comprised of different tokens, for example nonsense words or non-linguistic tone stimuli, to assess the contribution of phonological processing. Finally, artificial grammars with multiple levels of complexity can be used to quantify how well participants are able to learn increasingly complex rules, which may more closely reflect those in natural language grammars (Romberg and Saffran, 2013; Wilson et al., 2015).

The ability to process auditory sequences, even when stimuli are meaningless, is strongly linked with linguistic proficiency (Gómez and Gerken, 2000; Conway and Pisoni, 2008; Conway et al., 2010; Frost et al., 2015). Neuroimaging studies have demonstrated that artificial grammar processing engages a left-lateralised network of frontal, temporal and parietal brain areas similar to the set of regions involved in syntactic operations during natural language tasks (Friederici et al., 2000; Ni et al., 2000; Friederici and Kotz, 2003; Petersson et al., 2004; Forkstam et al., 2006; Friederici et al., 2006; Hickok and Poeppel, 2007; Bahlmann et al., 2008; Makuuchi et al., 2009; Folia et al., 2011; Friederici, 2011; Fedorenko et al., 2012; Petersson et al., 2012a, 2012b) and is associated with developmental language impairment (Evans

et al., 2009).

The sequence processing ability of patients with non-fluent aphasia has not been systematically compared across aetiologies. Non-fluent variant Primary Progressive Aphasia (nfvPPA), also variously known as Progressive Non-Fluent Aphasia (PNFA), nonfluent/agrammatic Primary Progressive Aphasia (naPPA), and Agrammatic Primary Progressive Aphasia (PPA-G), is an adult onset neurodegenerative aphasia characterised by agrammatism and speech apraxia (Gorno-Tempini et al., 2011). It is in many ways the neurodegenerative equivalent of Broca's aphasia, though some differences do exist in the pattern of speech output impairment (Patterson et al., 2006). The majority of cases are associated with primary tau pathology but a significant minority have TDP-43 related disease (Kertesz et al., 2005; Josephs et al., 2006; Knibb et al., 2006a, 2006b; Mesulam et al., 2014). nfvPPA typically leads to subtle structural neuroimaging changes in left inferior frontal and insular cortex (Gorno-Tempini et al., 2004), which correlate with clinical severity (Rogalski et al., 2011). Chronic non-fluent aphasia due to stroke (Broca's aphasia) results in a similar clinical phenotype of agrammatism and apraxia of speech. The left frontal tissue damage is stable, with partial clinical improvement over time (Kertesz and McCabe, 1977). The extent and pace of this improvement is variable and depends strongly on the integrity of the underlying white matter (Price et al., 2010; Seghier et al., 2016). Better understanding of the abilities of participants with similar symptoms arising from very different aetiologies could provide valuable insights into the neurobiological underpinnings of domain-general and language-related processes, and inform treatment strategies (Brownsett et al., 2014; Geranmayeh et al., 2014a, 2014b).

In the present study, patients with nfvPPA, non-fluent aphasia due to stroke, and matched controls were tested on their implicit learning of a mixed-complexity artificial grammar, combining sequencing relationships of increasing complexity using nonsense words or tones. We aimed to test the following linked hypotheses:

1) Rule acquisition differs when structurally identical sequences are comprised of nonsense words rather than non-linguistic tones.
2) Artificial grammar learning ability is similar in patients with vascular and neurodegenerative aphasia.
3) Grammatical impairments in aphasic patients are disproportionately greater for complex, configurational or hierarchical, sequencing operations.
4) Patients with aphasia can improve their ability to detect grammatical disruptions with repeated implicit training.

2. Methods

2.1. Participants

Three groups of participants were recruited. Demographics of the groups are outlined in Table 1. All patients were right handed. One control was left handed. Thirteen patients with mild to moderate nfvPPA were identified from specialist cognitive clinics led by authors JBR and TDG according to consensus diagnostic criteria (Gorno-Tempini et al., 2011). These criteria were strictly applied; particular care was taken to exclude non-fluent patients who had lexical

Table 1
Subject demographics. Mean (s.d., range). Age leaving education is reported as it is a better measure of highest scholastic attainment than number of years in study. No individuals were mature students.

	Control	nfvPPA	Stroke
Number	11	10	12
Age	69 (8, 54–79)	73 (7, 63–82)	60 (11, 33–74)
Age leaving education	18 (2, 15–22)	18 (3, 15–25)	20 (4, 15–26)
Years of musical training	2 (3, 0–10)	1 (1, 0–3)	3 (5, 0–13)