A verbal strength in children with Tourette syndrome? Evidence from a non-word repetition task

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Abstract

Tourette syndrome (TS) is characterized by motor and vocal tics, and frontal/basal-ganglia abnormalities. Whereas cognitive strengths have been found in other neurodevelopmental disorders, less attention has been paid to strengths in TS, or to verbal strengths in any neurodevelopmental disorder. We examined whether the finding of speeded TS production of rule-governed morphological forms (e.g., “slipped”) that involve composition (Walenski, Mostofsky, & Ullman, 2007) might extend to another language domain, phonology. Thirteen children with TS and 14 typically-developing (TD) children performed a non-word repetition task: they repeated legal phonological strings (e.g., “naichovabe”), a task that taps rule-governed (de)composition. Parallel to the morphology findings, the children with TS showed speeded production, while the two groups had similar accuracy. The results were not explained by potentially confounding factors, including IQ. Overall, the findings suggest that rule-governed grammatical composition may be speeded in TS, perhaps due to frontal/basal-ganglia abnormalities.

1. Introduction

Previous research on neurodevelopmental disorders has, not surprisingly, focused on the various impairments and weaknesses found in the disorders, and their underlying causes. However, studies have recently also begun to examine whether individuals with these disorders might have not only weaknesses, but also strengths, relative to typically-developing (TD) individuals. For example, research has revealed possible enhancements in auditory and visual perception or attention in individuals with autism spectrum disorder, as compared to TD controls (Mottron, Dawson, Soulie, & Burack, 2006; Remington, Swettenham, & Lavie, 2012). Similarly, strengths in visuo-spatial processing have been suggested for developmental dyslexia (Diehl et al., 2014; Schneps, Brockmole, Sonnert, & Pomplun, 2012). However, some other neurodevelopmental disorders, including Tourette syndrome (TS), have been less well studied with regard to potential strengths. In addition, there has been relatively little research suggesting strengths in the verbal domain in any neurodevelopmental disorder (Just, Cherkassky, Keller, & Minshew, 2004; Jarvinen-Pasley, Wallace, Ramus, Happé, & Heaton, 2008; Walenski, Mostofsky, Gidley-Larson, & Ullman, 2008; Walenski, Mostofsky, & Ullman, 2014), including in TS (Walenski, Mostofsky, & Ullman, 2007). Here we address these gaps by probing for potential verbal strengths in TS.

TS is a neurodevelopmental disorder characterized by multiple motor tics and at least one vocal tic that are not explained by medications or another medical condition (American Psychiatric Association, 2013). Tics, which can be expressed as simple or complex motor movements or vocalizations, are characteristically fast, abrupt, recurrent, and semi-voluntary (American Psychiatric Association, 2013). The tics are thought to be caused by disturbances of the basal ganglia and closely connected regions of cortex, especially motor and cognitive regions of frontal cortex (Albin & Mink, 2006; Müller-Vahl et al., 2014). Such disturbances are reflected in both structural and functional abnormalities of the basal ganglia and frontal cortex, and their connecting circuits (Müller-Vahl et al., 2014). These frontal/basal ganglia abnormalities, including hyperactive circuitry, have been posited to result in increased disinhibition of frontal activity, leading...
to tics and a hyperkinetic behavioral profile (Johannes et al., 2002; Zieman, Paulus, & Rothenberger, 1997).

Although most research has focused on delineating the impairments and weaknesses of TS (Murphy & Eddy, 2013), some studies have begun to examine strengths in the disorder. Thus far, strengths have been found in somewhat disparate domains and functions, and have not been consistently observed, or have been reported in a small number of studies.

First, some studies have reported TS advantages in what have been characterized as executive functions such as volitional control and task switching. For example, children with TS have been found to perform faster and/or more accurately than TD controls on mixed-trial anti-saccade tasks, which involve repeatedly switching between pro-saccade and anti-saccade trials, i.e., between eye movements towards vs. away from a target (Jackson, Mueller, Hambleton, & Hollis, 2007; Jung, Jackson, Nam, Hollis, & Jackson, 2014; Jung, Jackson, Parkinson, & Jackson, 2013; Mueller, Jackson, Ranu, Sophia, & Hollis, 2006). Speeded reaction times have also been observed on an analogous task involving hand instead of eye movements (Jackson et al., 2011). It has been argued that these findings may be explained by children with TS developing improved control abilities due to their constant efforts at tic suppression (Mueller et al., 2006). Some evidence has also been taken to suggest TS strengths at working memory updating (Thibault et al., 2008). However, other tasks probing executive functions, including working memory, have shown normal or even mildly impaired performance in TS, weakening the hypothesis that the disorder is associated with strengths in this domain (Channon, Gunning, Frankl, & Robertson, 2006; Mostofsky, Lasker, Singer, Dencikla, & Zee, 2001; Murphy & Eddy, 2013).

Second, we are aware of four studies that have reported strengths related to motor function or knowledge. One study found that children with TS showed faster movements than TD controls on a finger sequence task (Avanzino et al., 2011). This was found when performing the task both with the right hand only and bimanually, though the right hand condition was also associated with decreased accuracy. The results were taken to indicate altered organization of inter-hemispheric connections in TS. Another study found that individuals with TS showed faster and more force-efficient performance than controls in some (though not all) goal directed movements, with no accuracy differences (Georgiou, Bradshaw, Phillips, Cunnington, & Rogers, 1997). This was taken to reflect abnormal motor asymmetry due to abnormal basal ganglia. Yet another study found superior motor performance in combination with reward in TS, which was explained in terms of overactive dopamine transmission (Palminteri et al., 2011). A fourth study found that TS participants were faster (but not more accurate) than controls at naming manipulated objects such as hammer, but not non-manipulated objects such as elephant (Walenski, Mostofsky, & Ullman, 2007). Since knowledge of manipulated objects seems to involve motor skill knowledge learned in procedural memory (in contrast to non-manipulated objects, which may primarily involve conceptual knowledge learned in declarative memory; Ullman, 2007), the findings were attributed to atypically fast processing of knowledge learned in the procedural memory brain system.

Third, two studies have reported strengths in other domains. One study found superior TS performance (in both speed and accuracy) on one of four conditions in a time processing task (Vicario et al., 2010). The authors suggested that the results were consistent with enhanced cognitive control abilities. Another study reported enhancements in mental rotation (more correct responses in a 5 min. period, thus reflecting a combination of speed and accuracy) in females with TS relative to female TD controls, though it was impaired in males with TS relative to male controls (Alexander & Peterson, 2004). The results were discussed with regard to potential associations between elevated prenatal androgen levels and brain masculinization.

Overall, there seems to be little if any functional coherence to the TS strengths reported thus far. However, these strengths may all be related neurobiologically, in particular because all the types of tasks and functions for which TS strengths have been reported appear to depend on frontal and/or basal ganglia structures, and in most cases dopamine as well: control, task switching and other executive functions (Ravizza & Ciranni, 2002); working memory (Smith & Jonides, 1998); motor function and knowledge (Swinnen et al., 2010), including for naming manipulated objects (Ullman, 2007); procedural memory (Ullman, 2004); time processing (Ivry & Spencer, 2004); and mental rotation (Cohen et al., 1996). As discussed in greater detail in the Discussion, we suggest that the underlying neurobiology of TS that leads to rapid motor and verbal tics and a hyperkinetic behavioral profile may also lead to the speeded performance (and potentially greater accuracy as well) of a range of other processes that depend on the neurobiological substrates affected in TS, in particular frontal/basal ganglia circuits and related dopaminergic systems. In other words, the abnormal rapidity found in the clinical symptom of tics may extend to other functions that are not part of the clinical manifestation, due to their common reliance on abnormal frontal/basal ganglia circuits. We refer to this neurobiological account as the Clinical Extension Hypothesis.

If previously observed strengths may be best explained not by cognitive or functional accounts, but by the neurobiological abnormalities of frontal/basal ganglia circuits in TS, we would expect that other functions that depend on these circuits may show analogous strengths. A substantial body of work has linked aspects of language, in particular grammar, to frontal/basal ganglia structures and circuitry (for reviews, see Teichmann et al., 2015; Ullman, 2004, 2016). Our mental grammar underlies the rule-governed sequential and hierarchical combination of complex (compositional) linguistic representations, across grammatical subdomains, including syntax (in computing phrases and sentences; e.g., “the” + “cat”, noun phrase + verb phrase), morphology (in computing complex words, for example, in regular inflection; e.g., “walk” + “-ed”) and phonology (in novel word forms, whose phonological elements must somehow be combined according to the phonotactics of the language, i.e., according to the phonological grammar of the language). In particular, evidence suggests that grammatical rules whose learning depends on the basal ganglia are eventually processed in frontal structures, especially in Broca’s area and nearby cortex (e.g., Brodmann’s areas BA 44 and 6 Ullman, 2004, 2016). Thus grammatical processing – across syntax, morphology, and phonology – might also be expected to be speeded in TS.

Surprisingly, there has been very little research examining grammar in TS (a handful of studies have investigated other aspects of language in TS, though none have reported strengths; Legg, Penn, Temlett, & Sonnenberg, 2005). We are aware of no studies of either syntax or phonology and only one of morphology. Consistent with our hypothesis, this study reported speeded performance (Walenski et al., 2007). Children with TS and age- and sex-matched TD control children (aged 8–17) were tested on a past tense production task, in which participants were presented with verb stems (e.g., walk, dig), and were asked to produce their past tenses as quickly and accurately as possible. The verbs were of several types, including regulars (both existing and novel, e.g., slip, rich), and irregulars (both existing and novel, e.g., dig, sping). The group with TS was significantly faster than the TD group in producing regular past tenses (for both existing and novel regulars), which evidence suggests undergo rule-governed composition by the mental grammar (e.g., “slip” + “-ed”) and
depend on frontal/basal ganglia circuits (Pinker & Ullman, 2002; Ullman, 2004, 2016). In contrast, there were no group differences in response times in the production of irregular past tense forms, which evidence suggests are retrieved from (dug) or processed in (splung) associative memory (Pinker & Ullman, 2002; Ullman, 2004). Likewise, there were no group differences in “inconsistent” regulars (e.g., squeezed), which, like irregulars, appear to be retrieved from memory. There two groups did not differ in accuracy on any verb type. The authors argued that the speeded performance of only the rule-governed combined morphological forms (slipped, ricked) may reflect a broader pattern of speeded rule-governed grammatical composition in TS. Moreover, since independent evidence indicates that grammar, in particular rule-governed composition, is learned and processed in the procedural memory system, which is rooted in frontal/basal ganglia circuits (Ullman, 2004), it was suggested that the observed pattern might reflect speeded processing of knowledge learned in procedural memory more generally, that is, of both linguistic and non-linguistic knowledge. Indeed, the speeded performance observed at naming manipulated (and not non-manipulated) objects described above was found in the same participants (Walenski et al., 2007), underscoring the plausibility of this account.

The current study aims to advance the investigation of speeded grammar in TS by examining whether the speeded processing of morphology extends to another key domain of grammar: phonology, that is, the sound structure of words. In particular, if children with TS are faster at rule-governed grammatical combination in general, they should show not only speeded combination of morphological units, that is, of morphemes (“walk”+“-ed”), but also of phonological units, that is, phonemes or syllables.

In order to test whether the findings suggesting speeded TS composition in regular morphology might extend to phonology, we probed TS and TD participants on a non-word repetition task, in which participants hear and repeat aloud phonological sequences such as /tewasthajg/. These sequences do not exist as words in the language, and have no meanings (hence the term ‘non-words’), but generally follow the phonological grammar (phonotactics) of the language, in this case American English. The dependent measure in this task is typically accuracy.

The non-word repetition task taps language-related functions in the domain of phonology that seem to be analogous to those involved in morphology in the past-tense production of regulars (Walenski et al., 2007). Perhaps most importantly, like the production of regular past tenses, which appears to involve the rule-governed composition of morphemes (Pinker & Ullman, 2002; Ullman, 2004, 2016), the non-word repetition task also seems to involves rule-governed (de)composition, though in this case in the manipulation of phonological segments (e.g., phonemes or syllables). Participants do not simply repeat the novel sequence of phonemes as an unanalyzed whole. Rather, several lines of evidence suggest that they generally break it down into smaller phonological units, and then attempt to reconstruct the phonological sequence in their output, according to the phonotactics of the language.

First, evidence suggests that in non-word repetition individual segments (e.g., phonemes, diphones, or syllables) are accessed. In particular, studies have found that properties of individual segments affect task performance, which would not be expected if the string were simply repeated as an unanalyzed whole. For example, accuracy of repetition is modulated by phoneme type (e.g., coronal stops vs. coronal fricatives, Cleary, Dillon, & Pisoni, 2002), the presence of singleton consonants vs. consonant clusters (Gathercole & Baddeley, 1989) syllable type (real-word or not; e.g. BATHesis versus FATHesis; Dollaghan, Biber, & Campbell, 1995), and phoneme, diphone, and syllable frequency (Coady & Aslin, 2004; Coady, Evans, & Kluender, 2010; Tremblay, Deschamps, Baroni, & Hasson, 2016). Evidence also suggests that the position of a segment within the non-word string modulates performance at the task (Coady & Evans, 2008; Tremblay et al., 2016). Furthermore, Barry, Hardiman, and Bishop (2009) provided electrophysiological evidence of sensitivity to individual segments in a non-word repetition strings, while a recent fMRI study demonstrated neural sensitivity to syllable frequency in non-word strings in the task (Tremblay et al., 2016).

Second, evidence suggests that in non-word repetition individual phonological segments are not just accessed, but also stored in short-term/working memory. Non-word repetition accuracy correlates with accuracy at traditional measures of phonological short-term memory, such as digit span (which clearly involves individual units) (Adams & Gathercole, 2000). Additionally, length effects have been commonly reported for the non-word strings (i.e., strings with more segments are repeated less accurately than those with fewer segments), which has been interpreted as suggesting that longer strings constitute a greater load on short-term memory, due to the greater number of individual segments (Gathercole & Adams, 1994). Also, patients with auditory short term memory impairments have shown poor performance on the task, especially with longer items (Baddeley, Gathercole, & Papagno, 1998). Finally, the segments in the non-words show the same type of primacy and recency effects that are encountered in the serial recall of individual words or numbers, suggesting that they are maintained as individual units (Archibald & Gathercole, 2007b; Gupta, 2005).

Third, evidence suggests that individual segments are not only accessed and stored, but also manipulated. Error analyses of responses have revealed that migration errors, which entail reordering segments, suggesting the manipulation of phonemes, are common errors, as are addition, deletion, and substitution errors, also consistent with phoneme manipulation (Archibald & Gathercole, 2007a; Jones & Witherstone, 2011; Nakeva Von Mentzer et al., 2015). Furthermore, Archibald and Gathercole (2007a) found that migrations were more common in non-word repetition than in the repetition of syllable lists (matched to the non-words on syllable length and content), further supporting phoneme manipulation in non-word repetition.

Finally, evidence suggests that the re(composition) of the individual segments in non-word repetition is influenced by phonotactic rules. For example, at least in typically-developing children and adults, the output (i.e., the produced form) is modulated not only by the input sequence, but also by phonotactic rules in the speaker’s language (Coady & Evans, 2008). Along the same lines, non-words that follow the speaker’s phonotactic rules are repeated more accurately than those that do not, consistent with the task being sensitive to the phonotactics of the language (Munson, Kurtz, & Windsor, 2005; Nakeva Von Mentzer et al., 2015; Vitevitch, Luce, Charles-Luce, & Kemmerer, 1997).

Thus, overall, multiple lines of evidence suggest that non-word repetition generally undergoes decomposition and then recombination of phonological units, following the phonotactic rules of the language.

The similarity between non-word repetition and the production of regulars in past-tense production extends beyond their mutual dependence on rule-governed composition. In addition, both tasks probe rule-governed processing in oral production, even though they differ in the extent to which the stimulus is included in the target (fully in non-word repetition, and only partially in past tense production, in which participants need to add an –ed suffix). Moreover, both tasks seem to tap short-term memory. As we have seen above, evidence suggests that non-word repetition involves temporarily maintaining the disassembled phonological units in short-term memory. Similarly, recent evidence suggests that the morphemes seem to be retained in short term memory in the
processing of regular past tense forms (Walenski, Prado, Ozawa, Steinha, & Ullman, submitted for publication). Finally, more direct evidence also suggests that past tense production and non-word repetition are related, since performance at the two tasks has been found to correlate in typically-developing children (Christensen & Hansson, 2012).

The non-word repetition paradigm not only shows important similarities and overlap with the production of regulars in the past-tense production task, but also has the advantage of being widely used, particularly with neurodevelopmental disorders. Thus it is well understood, and allows for comparability among disorders. Performance at the task seems to be impaired in most neurodevelopmental disorders in which it has been examined, including specific language impairment dyslexia (Melby-Lervåg, Lyster, & Hulme, 2012), autism spectrum disorder (Tager-Flusberg & Joseph, 2003) and Down syndrome (Combain, 1999).

It has been less well studied in other developmental disorders. We are aware of one study in Attention Deficit Hyperactivity Disorder (ADHD), which did not find group differences (Redmond, Thompson, & Goldstein, 2011), and a handful of studies in Williams syndrome, which reported performance worse or similar to that of controls (Grant, Karmiloff-Smith, Berthoud, & Christophe, 1996). We are not aware of any studies examining the task in either Obsessive Compulsive Disorder (OCD) or Tourette syndrome. Importantly, there has been very little research on the task in neurodevelopmental disorders examining response time (in addition to accuracy) as a dependent measure, as was done in the present study (we are aware of only one study, which examined children who stutter, and found no group differences compared to typically-developing children; Sasisekaran & Byrd, 2013).

Two of the most widely used non-word repetition tests are the Children’s Test of Non-Word Repetition (CNRep; Gathercole, Willis, Baddeley, & Emslie, 1994) and the Non-word Repetition Test (NRT; Dollaghan & Campbell, 1998). Although seemingly similar, these differ in certain important respects. Of particular interest here, the characteristics of the NRT seem to be better suited for probing phonological combination. First of all, in the CNRep, quite a few items pose particular articulatory difficulties; as a result, performance may be especially affected by articulation, which is not of interest here, and could confound the results. This could be particularly problematic in TS, which has been associated with articulatory and fluency difficulties (De Nil, Sasisekaran, Van Lieshout, & Sandor, 2005). Specifically, the CNRep contains some items with complex consonant clusters (‘blonta’stei̯ni̯j’), and most items have weak syllables (which have reduced vowels; e.g., ‘hæmpant’, ‘tæflast’); both of these seem to pose articulatory difficulties that can affect non-word repetition performance (Coady & Evans, 2008). In contrast, the NRT contains no items with either complex consonant clusters or weak syllables. Rather all items contain simple CV(C) syllables, and have equal stress on each syllable – which has the added benefit of making the items acoustically salient. Second, in the CNRep many items include phonological sequences that correspond to existing words or morphemes (e.g., ‘pen’ in ‘penli’ or ‘-ing’ in ‘blonta’stei̯ni̯j’). This is problematic for testing phoneme (de)composition and manipulation, since these sequences could be treated as chunks rather than broken into individual phonological units. In contrast, the items in NRT were specifically selected not to contain any such phonological sequences.

The present study, which examined whether fast grammatical processing in TS might extend from morphology to phonology, tested children with TS and age- and sex-matched TD children on the NRT.

### 2. Methods

#### 2.1. Participants

Thirteen children diagnosed with TS, aged 8–16 years (Table 1), were recruited through the Child Neurology Outpatient Clinic at the Johns Hopkins Hospital. All met the diagnostic criteria defined by the Tourette syndrome Classification Group (1993), confirmed by a child neurologist (author S.H.M.). ADHD and OCD are common in TS (American Psychiatric Association, 2013), so children with these comorbidities were not excluded. Two of the children with TS met criteria for ADHD, as determined by the DICA-IV criteria (Reich, Welner, & Herjanić, 1997), and three met criteria for OCD, also determined by the DICA-IV criteria (one child had both ADHD and OCD). Seven of the 13 children with TS were taking psychoactive medication at the time of testing: one was taking haloperidol and fluvoxamine, 1 aripiprazole, 1 lamotrigine and fluvoxamine; 1 dextroamphetamine and clonidine; 1 methylphenidate and clonidine; 1 sertraline hydrochloride; 1 risperidone; and 1 pimozide and clonidine. The age range of the participants was determined by the age range in the past tense production article (Walenski et al., 2007), as well as patient availability. All children with TS were tested at the Kennedy Krieger Institute (KKI).

In addition, 14 typically-developing control children aged 8–15 were tested (Table 1). They were group-matched to the children with TS on age, handedness, and sex (ps > 0.5); full scale IQ differed between the groups (p < 0.05); these and other variables were considered as covariates in all analyses (see below). The control group was recruited through local schools and community-wide service groups. Five of the controls were tested at KKI and 9 at the Georgetown University Medical Center (GUMC). No control children had any known developmental or psychiatric disorders, and none had any history of tics; this assessment was based on parental report and the DICA-IV criteria (Reich et al., 1997) for children tested at KKI, and parental report and the Child Behavioral Checklist (Achenbach & Dumenci, 2001) for children tested at GUMC. Absence of ADHD was further confirmed with the Conners ADHD parent scale (Conners, 2008) and the DuPaul ADHD parent scale (DuPaul, Power, Anastopoulos, & Reid, 1998). None of the control children were taking psychoactive medication.

All children were monolingual native American-English speakers from the Washington- Baltimore area. Both right and non-right handed children were included (Oldfield, 1971). Full scale IQ was assessed with the Wechsler Intelligence Scale for Children – III (Wechsler, 1991), except for the 9 controls tested at GUMC, who were administered the Kaufman Brief Intelligence Test, second edition (Strauss, Sherman, & Spreen, 2006). The scores for these two tests are highly correlated (Strauss et al., 2006). The Institutional Review Boards of Johns Hopkins University and GUMC provided approval for this study. All participants provided written consent (caregivers) and assent (children) before testing, and received a copy of the consent form.

### Table 1

<table>
<thead>
<tr>
<th>Participant information</th>
<th>TS children (n = 13)</th>
<th>TD children (n = 14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Mean 11.87, SD 2.5</td>
<td>Mean 11.31, SD 2.1</td>
</tr>
<tr>
<td>Full Scale IQ (FSIQ)</td>
<td>Mean 101.46, SD 11.2</td>
<td>Mean 120.86, SD 10.6</td>
</tr>
<tr>
<td>Right handed</td>
<td>9</td>
<td>13</td>
</tr>
<tr>
<td>Male sex</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Comorbidities</td>
<td>ADHD 2; OCD 3</td>
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</tr>
<tr>
<td>Psychoactive medication</td>
<td>7 taking medication</td>
<td>None</td>
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2.2. Non-word Repetition Task

All children were tested on a modified version of the Non-word Repetition Test (NRT; Dollaghan & Campbell, 1998). In summary, the task consists of 16 test items that are phonetically legal in American English: four non-words at each of four syllable lengths (one, two, three, and four syllables), presented in order of increasing length. That is, the four one syllable non-words are presented first, followed by the two syllable non-words, and so on. All non-words begin and end with a consonant and contain no consonant clusters. Thus, 1-syllable non-words are consonant-vowel-consonant (CVC) sequences; 2-syllable non-words CV.CVC; 3-syllable non-words CV.CV.CVC; and 4-syllable non-words CV.CV.CV.CV.CVC. The 16 items were as follows (represented in IPA): /næb/, /voʊp/, /tæʊɡ, /dæf/, /tɛvək/, /tjʊvæɡɪ/, /nætəʊʃ/, /tʃi nɑətæʊt/, /nɑɪtʃʊvʊəb/, /dæʃʊmɔ/s/) with covariates was phonological length (\( \beta = 0.04 \), \( t(22.7) = 1.4, p = 0.19 \)), age (\( \beta = 0.28 \), \( t(22.3) = 2.4, p = 0.02 \)), and phonological length (\( \beta = -1.5, t(14.4) = 4.88, p = 0.0002 \)). For RT analysis, the only variable that was retained as a covariate in the final model with covariates was phonological length (\( \beta = 0.14, t(14.9) = 4.3, p = 0.0007 \)).

Below, we report type III F tests for the results of the fixed effect of group, with significance assessed at \( \alpha = 0.05 \). All \( p \) values are reported as two-tailed. In all analyses, degrees of freedom were computed using the Satterthwaite approximation.

3. Results

The children with TS did not differ from the TD control children on the accuracy of their responses in the Non-word Repetition Task; this result also held both without and with covariates included. See Table 2.

In contrast, analysis of response times indicated that the children with TS were significantly faster at producing non-words than the control children. This held in analyses both without and with covariates. See Table 3.

4. Discussion

This study tested children with TS and TD children on the Non-word Repetition Task (NRT) (Dollaghan & Campbell, 1998). The children with TS were faster than the TD children at initiating their responses in non-word repetition. This result held whether or not
Accuracy results from the Non-word Repetition Task.

<table>
<thead>
<tr>
<th></th>
<th>Group comparison: Analysis without covariates</th>
<th>Adjusted Means</th>
<th>Group comparison: Analysis with covariates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TS</td>
<td>TD</td>
<td>TS</td>
</tr>
<tr>
<td>Accuracy</td>
<td>82.2% (2.81)</td>
<td>81.7% (4.02)</td>
<td>82.6% (2.81)</td>
</tr>
</tbody>
</table>

Note. Mean accuracy (and standard errors in parentheses) are shown for each group. Mean percent correct scores shown here were computed for each subject and then averaged over all subjects in each group. See text for the covariates contributing to the adjusted means in the analysis with covariates. Adjusted means and standard errors from the logistic regression are presented as untransformed values. These can be transformed into probabilities of correct responses with the equation y = 1/(1 + e^{-x}), where x is the adjusted mean. Transformed probabilities are not shown here because standard errors are not transformable.

Table 3
Response time results from the Non-word Repetition Task.

<table>
<thead>
<tr>
<th></th>
<th>Group comparison: Analysis without covariates</th>
<th>Adjusted Means</th>
<th>Group comparison: Analysis with covariates</th>
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<tbody>
<tr>
<td></td>
<td>TS</td>
<td>TD</td>
<td>TS</td>
</tr>
<tr>
<td>lnRTs</td>
<td>5.98 (0.04)</td>
<td>6.44 (0.06)</td>
<td>5.99 (0.16)</td>
</tr>
</tbody>
</table>

Note. Mean natural-log (ln) transformed RTs (and standard errors in parentheses) are shown for each group. Means were computed for each subject and then averaged over all subjects in each group. Untransformed means: TS RTs: 442 ms (SD 41); TD RTs: 903 ms (SD 210). See text for the covariates contributing to the adjusted means in the analysis with covariates.
Why might composition be speeded in TS? One possibility is that speeded performance is specific to composition in grammar, including both morphology and phonology. However, the same TS participants who showed fast production of morphologically composed forms were also fast at naming manipulated (but not non-manipulated) objects, which was taken to suggest that children with TS may be fast at processing knowledge learned in procedural memory, including both linguistic and motor knowledge (Walenski et al., 2007). Although a TS account of speeded processing of knowledge learned in procedural memory seems plausible, an underlying neurobiological account is still needed. Moreover, procedural memory may not easily explain speeded performance in TS in tasks designed to probe various other aspects of cognition (see Section 1).

As discussed briefly in the Introduction, here we suggest that a neurobiological account may explain most if not all of the findings of speeded performance in TS, including those reported in the present study. In particular, we propose the neurobiologically motivated Clinical Extension Hypothesis. This posits that the speeded performance found for phonology (reported here) and morphology (Walenski et al., 2007), as well as the speeded performance (and perhaps increased accuracy; see below) observed in other tasks in TS (see Section 1), may be largely explained by neurobiological mechanisms that also result in clinical symptoms, in particular in the rapidity of the motor and verbal tics that characterize the disorder. That is, the rapidity of tics may extend to other functions that are not part of the clinical symptomatology, in particular functions that depend on the neurobiological substrates that are abnormal in TS and lead to tics.

As stated in the Introduction, a key characteristic of tics is their rapidity (American Psychiatric Association, 2013). Interestingly, it is less clear whether or not and to what extent tics are voluntary (Leckman, Bloch, Sukhodolosky, Scahill, & King, 2013). Although, not surprisingly, some evidence suggests that tics are different from voluntary movements (Obeson, Rothwell, & Marsden, 1981), recent research suggests that they are at least partially voluntary, being carried out to relieve sensory urges (Leckman et al., 2013; Puts et al., 2015). Thus, it is plausible that at least certain other processes might also be rapid in TS, even if they do not show evidence of the apparently involuntary nature of tics. Tics may therefore simply be the clinical tip of the iceberg of rapidity.

We suggest that any motor or cognitive processes that depend on the neurobiological substrates that underlie tics, in particular that underlie their rapidity, could potentially also be speeded. Although these neurobiological substrates are not fully elucidated, they are beginning to be understood. As discussed in the Introduction, abnormalities of frontal/basal ganglia circuits and dopamine are clearly implicated in the disorder, including in tics. Indeed, an important model of TS posits an imbalance between the direct and indirect pathways within the basal ganglia that leads to the increased disinhibition of frontal (and other regions) to which the basal ganglia project, via the thalamus, accounting for the tics and hyperkinetic profile of the disorder (Albin & Mink, 2006; Mink, 2006). Various lines of evidence support this view (Heise et al., 2010; Kalanithi et al., 2005; Kataoka et al., 2010; McCain, Bronfeld, Belelovsky, & Bar-Gad, 2009). Additionally, individuals with TS may show enhanced structural and functional connectivity both in frontal/basal ganglia circuits and within frontal cortices, with the abnormalities associated with increased frontal activity and the hyperkinetic/tic profile (Wang et al., 2011; Worbe et al., 2012, 2015).

As indicated in Section 1, all of the functions and tasks for which speeded (or in some cases more accurate) performance, has been observed, including morphology and phonology, depend on frontal and/or basal ganglia structures, and in many cases dopamine as well. Importantly, this also holds for non-word repetition and related tasks (Kalm & Norris, 2014; Liegeois, Morgan, Connelly, & Vargha-Khadem, 2011; Papoutsi et al., 2009; Peeva et al., 2010; Strand, Forsberg, Klingberg, & Norrelgen, 2008). Moreover, children with TS appear to have faster speech rates than TD children (De Nil et al., 2005), and speech production also depends on these structures (Munhall, 2001). Overall, these data lend support to the hypothesis that the frontal/basal ganglia and dopaminergic abnormalities in TS may underlie not only the tics and hyperkinetic profile, but also the rapid processing reported for a variety of tasks in the disorder, including non-word repetition.

Importantly, we do not expect that all tasks and functions that depend on frontal/basal ganglia circuits should show speeded processing. First of all, for a process to be speeded it would presumably have to have the potential to be speeded (e.g., unlike working memory capacity), and depend on the frontal/basal ganglia circuits in such a way that enable speeded processing (the specifics of which remain to be determined). Note that increased accuracy may also be expected in at least some cases: greater accuracy can result from speeded processing, since accuracy is generally determined with a time cutoff, so slow responses are also often counted as incorrect. Conversely, it is also possible that in some cases in TS the disinhibition of frontal structures might result in actual errors, as has been suggested for patients with Huntington’s disease, for example in their production of multiply affixed regular past tense forms such as slippeded (Ullman et al., 1997). It is not clear why such errors have not been observed in TS; future studies may elucidate this.

Second, not all portions of the basal ganglia are abnormal. One might expect only those functions that depend on frontal/basal ganglia “loops” whose underlying frontal and/or basal ganglia circuitry is abnormal to be affected. Motor and pre-motor regions, as well as Broca’s area, have all been found to be abnormal in TS and linked to tics (Müller-Vahl et al., 2014; Stern et al., 2000; Wang et al., 2011), suggesting that various aspects of motor and language function, including procedural memory (Ullman, 2004), might be speeded in TS.

Indeed, most of the speeded behaviors found in TS could in principle be due to just a few underlying functions, including potentially procedural memory. Speeding of skills learned in this system could explain observed findings of rapid morphological and phonological processing, as well as the speeding of naming manipulated objects, complex motor tasks, goal-directed movement, and mental rotation (Ullman & Pierpoint, 2005). Note that while some studies have suggested that learning in procedural memory may be impaired in TS (Keri, Szlobodynyik, Benedek, Janka, & Gadoros, 2002; Marsh et al., 2004), other studies have found no differences, or even enhanced learning (Nemeth et al., 2015). Even if procedural learning turns out to be impaired in TS, this does not preclude the possibility of speeded processing of the knowledge learned in this system. Indeed, given the disinhibition of frontal structures in TS, together with evidence suggesting that whereas learning skills in procedural memory relies heavily on the basal ganglia, once learned they are processed in frontal structures (Ashby, Turner, & Horvitz, 2010; Doyon et al., 2009), it is not unreasonable that only processing of well-learned skills in this system would be speeded.

The present findings and proposed neurobiological account for speeded behaviors in TS have various implications and potentially open new avenues of research. First of all, the finding of speeded non-word repetition and other speeded tasks in TS may also be observed in other disorders, especially those that are comorbid with TS, involve frontal and/or basal ganglia abnormalities, and are associated with symptoms that may be related to tics (e.g., stereotypies, obsessions, or impulsivity) – for example, autism spectrum disorder, OCD, and ADHD (Bradshaw, 2001). Indeed, some evidence suggests speeded processing in some of these disor-
ders (Just et al., 2004; Mavrogiorgou et al., 2002; Morault, Bourgeois, Laville, Bensch, & Paty, 1997; Walenski et al., 2014). For example, children with high functioning autism have been found to show the same pattern of speeded morphology as children with TS (Walenski et al., 2014). Interestingly, evidence also suggests speeded behaviors in Huntington’s disease (Beste, Humphries, & Saft, 2014), consistent with the hyperkinetic profile of the disorder.

Second, more generally, the Clinical Extension Hypothesis may warrant investigation in other disorders for characteristics beyond rapid processing. According to this neurobiological hypothesis, the characteristics of any symptom in any disorder could potentially extend to other functions that are not part of the clinical manifestation of the disorder, but depend on the neurobiological substrates that are abnormal in the disorder and lead to the clinical symptoms. Although in many cases this might simply lead to more subtle (non-clinical) deficits in other functions or domains, it some cases it might lead to unexpected behaviors, such as speeded processing, and perhaps even strengths.

Third, the present study addresses certain gaps in the non-word repetition literature. To our knowledge, this is among the first studies to examine response times (not just accuracy) in non-word repetition in neurodevelopmental disorders, and the first to examine the task in any form in TS. It also seems to be the first to identify an apparent strength (speeding) in the non-word repetition task in any disorder. It may behove future studies to examine response times in this and related tasks in a variety of neurodevelopmental and other disorders. More generally, the findings underscore the usefulness of investigating response times, and suggest that accuracy may sometimes be too crude a measure to detect atypical language processing (Walenski et al., 2014).

Fourth, the findings may have clinical implications. In particular, given that performance on non-word repetition seems to be impaired in most other neurodevelopmental disorders (at least as measured by accuracy), this test could potentially be used as an early diagnostic or predictor of TS in at-risk children (e.g., those with TS in their family) – especially since the onset of tics is usually later (around the age of 6 years of age; Singer, 2013) than the age at which non-word repetition abilities have been tested (as young as two; Coady & Aslin, 2004). Note that non-word repetition relies on imitation, a natural behavior even in infants.

Fifth, the results warrant examination in other domains, both in language (e.g., syntax), as well as other functions, including those that might rely on procedural memory, or whose functional anatomy overlaps that of the abnormalities seen in TS.

Finally, future work should investigate whether the findings reported here could translate into actual advantages for children or adults with TS, including in everyday life. After all, speeded language (or motor or cognitive functions) do not necessarily provide benefits. Some work in this direction has already been carried out for strengths in other disorders (Abraham, Windmann, Siefen, & Daum, 2006), though not in TS.

Of course, the present study also has limitations. First, the non-word repetition task does not have a control condition (i.e. real word repetition), and we did not assess neurobiological parameters of this task. Second, although in the present study the children with TS were faster than the TD children at initiating their responses, it remains to be seen whether or not the children with TS also took less time to complete their responses. Third, at least some studies show no RT or accuracy advantage in TS patients in tasks that involve basal ganglia circuits and could potentially be speeded, such as fine motor skills (Bloch, Sukhodolsky, Leckman, & Schultz, 2006). The hypothesis suggested here therefore needs to be treated with caution and tested in future research.

In conclusion, this study has presented evidence of speeded phonological processing, perhaps specifically in phonological com-

position, in children with TS. This reveals a new area of potential strength in TS, which may also warrant examination in related disorders. We have proposed an underlying neurobiological account for these and other speeded behaviors in TS. This account, the Clinical Extension Hypothesis, posits that the rapidity of tics may extend to other functions, due to their common reliance on abnormal frontal/basal ganglia circuits. Although the hypothesis clearly requires further investigation, it provides a promising theoretical framework for the study of strengths in TS, and possibly in related disorders.

References


