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Speaking-related changes in cortical functional connectivity associated with assisted and spontaneous recovery from developmental stuttering

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ABSTRACT

We previously reported speaking-related activity changes associated with assisted recovery induced by a fluency shaping therapy program and unassisted recovery from developmental stuttering (Kell et al., Brain 2009). While assisted recovery re-lateralized activity to the left hemisphere, unassisted recovery was specifically associated with the activation of the left BA 47/12 in the lateral orbitofrontal cortex. These findings suggested plastic changes in speaking-related functional connectivity between left hemispheric speech network nodes.

We reanalyzed these data involving 13 stuttering men before and after fluency shaping, 13 men who recovered spontaneously from their stuttering, and 13 male control participants, and examined functional connectivity during overt vs. covert reading by means of psychophysiological interactions computed across left cortical regions involved in articulation control.

Persistent stuttering was associated with reduced auditory–motor coupling and enhanced integration of somatosensory feedback between the supramarginal gyrus and the pre-frontal cortex. Assisted recovery reduced this hyper-connectivity and increased functional connectivity between the articulatory motor cortex and the auditory feedback processing anterior superior temporal gyrus. In spontaneous recovery, both auditory–motor coupling and integration of somatosensory feedback were normalized. In addition, activity in the left orbitofrontal cortex and superior cerebellum appeared uncoupled from the rest of the speech production network.

These data suggest that therapy and spontaneous recovery normalizes the left hemispheric speaking-related activity via an improvement of auditory–motor mapping. By contrast, long-lasting unassisted recovery from stuttering is additionally supported by a functional isolation of the superior cerebellum from the rest of the speech production network, through the pivotal left BA 47/12.

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1. Introduction

Developmental stuttering is a speech disorder that often requires considerable attention and heavy rehabilitation if children do not spontaneously recover. This speech disorder is neurobiologically characterized by an over-activation of right hemispheric brain areas during speech production (Belyk, Kraft, & Brown, 2015; Brown, Ingham, Ingham, Laird, & Fox, 2005; Budde, Barron, & Fox, 2014; Kell et al., 2009; Neumann et al., 2003). Several behavioral stuttering therapies exist that promise a reduction in symptoms. However, relapses are frequent (Bloodstein & Bernstein Ratner, 2008, pp. 384–386), suggesting that therapy-induced plasticity cannot support full recovery. Rarely, adults who stutter recover spontaneously, i.e. without any therapeutic intervention (Finn, 2004). Exploring these rare cases of recovered adults who have stuttered in the past (RS) using neuroimaging and comparing them with adults who persisted in stuttering (PS) before and after stuttering therapy as well as with fluent control participants may provide crucial information about the type of plasticity that is required for long-term recovery.

We previously reported brain activity during overt reading in the aforementioned groups, and observed that a fluency shaping therapy program that softens speech onsets, slows speech down, and modulates prosody abolished right-hemispheric over-activations and re-lateralized activity to a functionally normalized left hemisphere in male PS (Kell et al., 2009). Unassisted recovery in male RS was specifically associated with activation of the left BA 47/12, at the border between the orbital part of the inferior frontal gyrus (IFG) and orbitofrontal cortex. These findings, however, did not permit to fully apprehend the neural underpinnings of optimal recovery, as we did not report recovery-related changes in functional connectivity. Neuroplasticity is often associated with changes in the interaction between brain areas that complement changes in regional activity. Comprehensive interpretation of recovery-associated changes indeed requires taking into account changes at the level of inter-regional functional connectivity.

Several functional connectivity studies have already been performed in PS, either during speaking (Chang, Horwitz, Ostuni, Reynolds, & Ludlow, 2011; Lu et al., 2010; Watkins, 2011) or while resting silently inside the scanner (Lu et al., 2012; Sitek et al., 2016; Yang, Jia, Siok, & Tan, 2016). Both approaches have their advantages and drawbacks. Speaking constitutes a controlled experimental condition, yet it represents a state-dependent measure that can potentially be affected by articulation and by the influence of the scanning conditions on fluency (e.g., fluency induction due to the masking effect (Bloodstein & Bernstein Ratner, 2008, pp. 295–296 and pp. 392–393) by scanner noise). Resting state measurements are appealing because they potentially unravel trait-dependent differences. Yet, during resting state, subjects do not necessarily enter a consistent 'default mode', because participants may differ largely in covert behavior or vigilance (Tagliazucchi & Laufs, 2014). Altogether, functional connectivity studies in adults who stutter revealed abnormal connectivity between Broca's region and the premotor cortex (Chang et al., 2011) or the rest of the resting state language network in the bilateral fronto-temporo-parietal cortex (Lu et al., 2012), reduced auditory-motor coupling (Watkins, 2011), a hyper-connectivity in right homologue areas (Chang et al., 2011), and enhanced, compensatory cerebello-orbitofrontal connectivity (Sitek et al., 2016). Auditory-motor hypo-connectivity was confirmed in boys who stutter together with connectivity changes of the putamen (Chang & Zhu, 2013).

To our knowledge, only one study investigated therapy-associated changes in functional connectivity (Lu et al., 2012). In this study, therapy focused on changing the manner of speaking. Therapy reduced resting state functional connectivity between the superior cerebellum and the rest of the resting state language network, suggesting that intensive stuttering therapy uncoupled the superior cerebellum from language processing even during (covert speech in) the resting session.

Here, we re-analyzed the data from our previous study and investigated the connectivity changes associated with speech articulation in persistent stuttering, assisted recovery by a fluency-shaping intensive therapy that restructures speech as a whole (global speech restructuring), and by spontaneous recovery in adulthood. We focused on connectivity changes in the left hemisphere, where we previously observed plastic changes in assisted and spontaneous stuttering recovery (Kell et al., 2009). Based on these former experimental findings and on theoretical observations that parameter changes in both the feedforward control system and the auditory-motor mapping in the GODIVA model (Bohland, Bullock, & Guenther, 2010) induce dysfluencies (Civier, Bullock, Max, & Guenther, 2013; Civier, Tasko, & Guenther, 2010), we hypothesized that neuroplasticity associated with recovery should translate into connectivity alterations in these components. While connectivity changes in assisted recovery point to the way therapy reduces symptoms, findings in spontaneous recovery may reveal how neuroplasticity remedies stuttering in the long-term. In this regard, the functional connectivity of the only region that specifically activated in RS, namely BA 47/12, was of interest.

We investigated psychophysiological interactions (PPI) reflecting the functional connectivity between brain regions that is modulated by a psychological factor. In our case, we used the contrast overt > covert reading as psychological variable, which centers the analyses on sensorimotor aspects of articulation and controls for visual input (reading) of linguistic material. We compared speaking-related PPI maps of untreated PS compared to fluent controls to identify the abnormal functional connectivity profile in our sample of male adults who stutter. We subsequently studied therapy-induced changes in functional connectivity of PS and the connectivity profile associated with spontaneous recovery in RS compared to fluent controls.

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