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Dynamic changes of resting state connectivity related to the acquisition of a lexico-semantic skill

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ABSTRACT

The brain undergoes adaptive changes during learning. Spontaneous neural activity has been proposed to play an important role in acquiring new information and/or improve the interaction of task related brain regions. A promising approach is the investigation of resting state functional connectivity (rs-fc) and resting state networks, which rely on the detection of interregional correlations of spontaneous BOLD fluctuations.

Using Morse Code (MC) as a model to investigate neural correlates of lexico-semantic learning we sought to identify patterns in rs-fc that predict learning success and/or undergo dynamic changes during a 10-day training period. Thirty-five participants were trained to decode twelve letters of MC. Rs-fMRI data were collected before and after the training period and rs-fc analyses were performed using a group independent component analysis.

Baseline connectivity between the language-network (LANG) and the anterior-salience-network (ASN) predicted learning success and learning was associated with an increase in LANG – ASN connectivity. Furthermore, a disconnection between the default mode network (DMN) and the ASN as well as the left fusiform gyrus, which is critically involved in MC deciphering, was observed.

Our findings demonstrate that rs-fc can undergo behaviorally relevant changes within 10 training days, reflecting a learning dependent modulation of interference between task specific networks.

1. Introduction

Learning is based on experience, memory and adaptation. Changes in the way the brain processes new stimuli, accompanied by an improvement in goal-directed performance, are often referred to as 'neuroplasticity'. Practicing and learning are thought to both induce and profit from neuroplasticity, which has been described on different levels of neural organization, ranging from synaptic plasticity (Trachtenberg et al. 2002) to changes in complex neural circuitry (van Turennout et al., 2000). Modern brain imaging techniques have enabled the detection of macro-changes in task related brain function associated with various types of learning, such as motor, perceptual and associative learning (Kelly and Garavan 2005). A fairly new approach to the understanding of neuroplastic adaptation is based on the investigation of resting state functional connectivity (rs-fc) and resting state networks, where, in the absence of a task, interregional correlations of spontaneous low frequency BOLD fluctuations are calculated, which are thought to reflect synchronized neural activity (Biswal et al. 1995; Biswal 2012). Using rs-fc analyses a number of networks have been identified that resemble the patterns of activation observed during specific tasks; as such it is likely that rs-fc serves a dynamic role in brain function supporting the integration and consolidation of previous experience (Lewis et al. 2009). The translation of previous experience, e.g. training, into the

Abbreviations: ASN, anterior salience network; BA, brodmann area; BOLD, blood oxygen level dependency; DMN, default mode network; FNC, intercomponent functional connectivity; FDR, false discovery rate; fMRI, functional magnetic resonance imaging; FWE, family wise error; ICA, independent component analysis; iFC, intra-component functional connectivity; IFC, inferior frontal cortex; IPL, inferior parietal lobule; LANG, language network; MC, Morse Code; OTC, occipito-temporal cortex; rs-fc, resting state functional connectivity; SEM, standard error of mean; SMA, supplementary motor area

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modification of resting state networks is currently under extensive investigation and is likely to provide new insights into the neurobiological underpinnings of adaptation.

A number of studies have already demonstrated relationships between behavior and rs-fc measures, such that inter-individual differences in performance or traits are associated with differences in connectivity strength in networks related to the task and/or behavior (Wang et al. 2010). With respect to practicing and learning there is an increasing interest to longitudinally monitor changes in connectivity and network properties during a practicing/learning process, and to identify markers that allow for the prediction of learning success at baseline, i.e. prior to the training period. Some work in this regard has been done on motor and perceptual learning (Lewis et al. 2009; Ma et al. 2011; Baldassarre et al. 2012; Powers et al., 2012; Guidotti et al. 2015; Ventura-Campos et al. 2013; Albert et al. 2009; Sami, Robertson, and Miall 2014). However, only a few studies have looked at "higher" cognitive abilities involving a lexical and/or semantic learning process. Looking at reading competence, Horowitz-Kraus et al., (2015) for example could demonstrate that a specific reading-training program for children with and without reading difficulties, led to increases in rs-fc between the visual and attention network, as well as between the visual and executive function networks that correlated positively with word reading and reading comprehension (Horowitz-kraus et al. 2015). Likewise Murdaugh et al. found that a reading intervention in children with autism led to an increase in rs-fc between Broca's and Wernicke's areas and that the improvement in reading comprehension correlated with the increase in connectivity of these regions with the reading network (Murdaugh, Maximo, and Kana 2015).

To our knowledge rs-fc has not been investigated in the context of semantic and/or lexical learning, where study participants have to learn new stimulus – response associations. In the current study we used fMRI and Morse Code (MC) to investigate changes in rs-fc related to the newly acquired skill to decode sequences of short and long signals as letters. MC, a method of transmitting text information as a series of on-off tones, clicks, or flashes of light with different durations (short and long), provides an interesting model to investigate neural correlates of lexico-semantic learning and to probe the reading network. We recently introduced a learning paradigm using MC to investigate changes in neural activity related to the decoding of three-letter-words. Study participants learned to assign letters to certain sound pattern (pattern-to-letter/phoneme conversion), thereby establishing a link between an acoustic pattern and an already existing letter representation system. Specific brain regions are known to be critically involved in lexical and semantic processing were recruited in the learning process, such as the left inferior frontal cortex (IFC) and the left occipitotemporal cortex (OTC), including the fusiform gyrus.

With a focus on a network perspective to further analyze the underlying neural correlates of lexico-semantic learning, we now used rs-fMRI and independent component analysis (ICA) to identify characteristics in rs-fc and changes thereof that were related to both the learning process itself and to learning success. ICA allows the identification of a number of distinct resting state networks that have been attributed to various tasks. We hypothesized that there would be an association between task performance (after the learning process) and the connectivity (and changes thereof) between the language network (LANG) and the (anterior) salience network (ASN) on the one hand, and also a disconnection between the LANG and the default mode network (DMN).

2. Methods

2.1. Subjects

Thirty-five healthy, right-handed subjects (mean age 24 years, SD=2.7, 14 females) participated in the study. 18 subjects were drawn from the study previously published by Schlaffke et al. (2015) were also rs-fMRI data had been acquired. Another 17 subjects had participated in a new study where exactly the same study design had been used. In the new study participants had also practiced to transmit MC (5 min per session), in addition to the decoding part, which was identical in both groups (see below for details). The task related fMRI of this second group will be reported elsewhere. All subjects had normal or corrected-to-normal vision. Furthermore, no participant had a hearing impairment and all participants were tested for a normal hearing range of 20–20,000 Hz frequencies (Seikel et al., 2009). The study was conducted in accordance with the Declaration of Helsinki and was approved by the ethics committee of the Faculty of Psychology at the Ruhr-University Bochum, Germany. Before the experiment, participants were informed about the testing procedure and gave written informed consent.

2.2. Task and training

Morse Code (MC) is a method of transmitting text information as a series of on-off tones, clicks, or lights. The International Morse Code encodes the ISO basic Latin alphabet, some extra Latin letters, the Arabic numerals and a small set of punctuation and procedural signals as standardized sequences of short and long signals pictured as 'dots' (•) and 'dashes' (–), where the duration of a dash is three times the duration of a dot.

All participants were naïve to MC prior to the learning intervention. The learning procedure has been described in detail in (Schlaffke et al. 2015). In brief, using an in house developed audio book a subset of 12 letters (day 1: E S N and O; day 2: T and R; day 3: U and D; day 4: A and I; day 5: M and G; day 6: repetition of all letters) was presented and learned at a standardized speed. The audio book was played on a Google Nexus 7 tablet with the implemented "Google Play Music" presentation software. Stereo headphones by Philips (40mm speaker driver, 20–20000 Hz frequency range, 98 dB sensitivity, 32 Ω impedance, 500 mV maximum power input; lightweight comfort with adjustable headband) were used.

Study participants learned 12 letters in a specific order within six supervised learning sessions (duration per session approx. 60 min). In the first training session, participants learned to decipher four letters (E, N, O, S). On all training days, apart from the first, a repetition of the previously learned Morse Code letters was performed, followed by the practice of two new letters and the decoding of three-letter MC-trains. Participants of the second cohort ($n=17$) skipped decoding 30 (of 240) acoustically presented MC letters and practiced to transmit them instead. Except for this difference, both groups followed exactly the same learning protocol (same practicing time). The training was completed within ten days, with an adjournment of one weekend.

2.3. fMRI – sequences

All participants underwent two MRI sessions in a Philips Achieva 3T X-series MR-Scanner, one at the beginning (before the first training session) and one at the end (after the last training session). Using a 32 Ch head coil, in the first session high-resolution T1-weighted data sets (TR 8.3 ms, TE 3.8 ms, FOV 256 × 256, yielding 220 transversal slices with a voxel size of $1.00 \times 1.00 \times 1.00\ mm^3$ and reconstructed to $0.94 \times 0.94 \times 1.00\ mm^3$)