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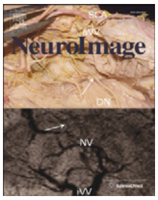

Robustness of intrinsic connectivity networks in the human brain to the presence of acoustic scanner noise

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ABSTRACT

Evoked responses in functional magnetic resonance imaging (fMRI) are affected by the presence of acoustic scanner noise (ASN). Particularly, stimulus-related activation of the auditory system and deactivation of the default mode network have repeatedly been shown to diminish. In contrast, little is known about the influence of ASN on the spontaneous fluctuations in brain activity that are crucial for network-related neuroimaging methods like independent component analysis (ICA) or functional and effective connectivity analysis (ECA). The present study assessed the robustness of intrinsic connectivity networks in the human brain to the presence of ASN by comparing 'silent' (sparse) and 'noisy' (continuous) acquisition schemes, both during task performance and during rest. In agreement with existing literature, ASN strongly diminished conventional evoked response levels. In contrast, ICA and ECA robustly identified similar functional networks regardless of the scanning method. ASN affected the strength of only few independent components, and effective connectivity was hardly sensitive to ASN overall. However, unexpectedly, ICA revealed notable differences in the underlying neurodynamics. In particular, low-frequency network oscillations dominated in the commonly used continuous scanning environment, but signal spectra were significantly flatter during the less noisy sparse scanning runs. We tentatively attribute these differences to the ubiquitous influence of ASN on alertness and arousal.

Introduction

Many studies have characterized the influence of the acoustic environment on various types of processing in the human brain. In the context of neuroimaging research, the confounding effect of the loud acoustic scanner noise (ASN) that occurs during gradient switching in functional magnetic resonance imaging (fMRI) has received particular attention (Bandettini et al., 1998; Talavage et al., 1999; Amaro et al., 2002; Moelker and Pattynama, 2003). It has repeatedly been shown that blood oxygenation level dependent (BOLD) activation contrasts in response to sound stimuli typically decrease throughout the auditory system, due to a combination of elevated baseline activity and saturated hemodynamic responses (Scarff et al., 2004; Langers et al., 2005b; Gaab et al., 2007). Furthermore, other brain systems that are not nominally involved in sound processing can be affected by ASN, including those related to vision (Zhang et al., 2005), motion (Cho et al., 1998; Fuchino et al., 2006), nociception (Boyle et al., 2006), working memory (Tomasi et al., 2005), or the default mode network (Gaab et al., 2008).

So far, the effects of ASN were studied exclusively in the context of task-related responses. In recent years, novel experimental designs have been developed for fMRI that do not rely on controlled task performance, enabling measurement during diverse paradigms, naturalistic behavior, or rest. This development has been made possible by the emergence of multivariate analysis techniques that do not require prior models of stimulus-evoked brain activity. As a case in point, one may consider the numerous measures related to functional and effective brain connectivity (Friston, 1994; Horwitz et al., 2005; Rogers et al., 2007; Cole et al., 2010). These methods typically operate by identifying similarities in the functional dynamics of large sets of voxels or multiple regions of interest (ROIs). Observed covariations can arise as a result of joint responses to imposed stimuli or tasks, but may likewise emerge when interacting brain regions react to each other's spontaneous activity.

Functional and effective connectivity methods have consistently revealed networks in the human brain that show coherent patterns of activity. Similar intrinsic connectivity networks have been found in a variety of tasks, and various networks persist even during rest (Damoiseaux et al., 2006; Fox and Raichle, 2007; Smith et al., 2009). Such resting state networks are thought to arise due to the presence of predominantly low-frequency spontaneous variations in brain activity (Cordes et al., 2001; Fransson, 2005; Auer, 2008). The origin of these slow but coherent neural fluctuations is not well understood. Some

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networks are thought to be driven by internal mental processing, like the default mode network (Raichle and Snyder, 2007). Still, it seems reasonable to assume that sensory information contributes to drive such networks or to modulate their ongoing activity (Grossberg, 1999; Friston, 2009). With that in mind, intrusive ASN may well influence the activity of intrinsic brain networks during rest, even if these are not nominally associated with sound processing. Yet, despite its potentially widespread influence on spontaneous brain activity in fMRI, the presence of ASN has so far largely been neglected in the context of functional connectivity analyses.

At first glance, the same issues that play a role in conventional behavioral paradigms may also occur in resting state studies. Connectivity measures quantify the presence of coherent fluctuations in brain activity, whether evoked or spontaneous. If brain systems are driven into a state of constant activity by the presence of ongoing ASN, the acquired BOLD fMRI signals may conceivably saturate near a fixed ceiling (Langers et al., 2005b). This might result in less signal variation, rendering relationships regarding functional behavior more difficult to detect. However, contrariwise, ASN might also augment the magnitude of neural fluctuations when taking modulatory interactions into consideration. For instance, whereas the auditory cortex might show little activity in the absence of any acoustic stimulation, in the presence of ASN its activity could be high when the subject is attending to the acoustic environment but lower when the subject is focusing on other input (Woods et al., 2009). Thus, ASN might enlarge the range of occurring signal variations by acting as a source of stimulation that may subsequently be subjected to sensory gating (Campbell et al., 2007; Mayer et al., 2009). In conventional approaches that model stimulus-evoked activity only, these modulations would not be registered unless they correlate with the experimental protocol. However, connectivity measures are sensitive to all sources of coherent signal variations, and may benefit from their presence.

In contrast with the prevailing notion that ASN primarily reduces sound-related responses in auditory processing centers alone, we entertain the option that ASN alters both spontaneous and evoked fluctuations in activity in much more widespread brain networks than previously thought. Our working hypothesis is that ASN broadly influences the observable functional relationships between brain regions, and that functional connectivity levels may be either increased or decreased in the presence of ASN compared to those in a more silent environment.

So far, intrinsic connectivity networks in fMRI have almost exclusively been studied with noisy scanning methods. The current study was set up to investigate the effects of the accompanying ASN on the outcomes of various functional and effective connectivity measures in healthy subjects. In addition to conventional noisy acquisition schemes, sparse scanning methods were employed that are commonly used to mitigate the effects of ASN in dedicated study designs (Hall et al., 1999). We considered not only the central auditory system but also other intrinsic brain networks, both in task-related and resting state designs.

Materials and methods

Subjects

Twelve healthy subjects (7 M, 5 F; mean 25 y, range 21–35 y) were invited to participate in this fMRI study on the basis of written informed consent, in approved accordance with the requirements of the institution's medical ethical committee. All subjects were right handed (Oldfield, 1971). They reported no history of auditory, neurological, or psychiatric disorders. Standard clinical audiometry was performed to confirm that all subjects had normal hearing. Hearing thresholds amounted to 11 ± 6 dB HL (mean ± SD; averaged over all subjects, both ears, and frequencies of 250–8000 kHz). One subject was excluded after data preprocessing because of excessive head motion due to urinary urges during the imaging session.

Data acquisition

Subjects were placed supinely in the bore of a 3.0-T MR system (Philips Intera, Best, the Netherlands), which was equipped with a standard 8-channel phased-array (SENSE) transmit/receive head coil. The functional imaging session consisted of eight runs of almost 7 min duration, each consisting of a dynamic series of identical T_2^*-sensitive whole-brain multislice gradient/field-echo echo-planar imaging (EPI) volume acquisitions (TE 23 ms; TA 2.0 s; FA 90°; matrix 64×64×48; resolution 3.0×3.0×3.0 mm^3; EPI factor 25; interleaved slice order, no slice gap). Initial preparation scans were used to achieve stable image contrast and to trigger the start of stimulus delivery, but these were not included in the analysis. Subjects wore ear plugs and a headset to dampen the ASN to approximately 70 dB SPL. The scanner coolant pump and fan were turned off during imaging to further diminish ambient noise levels.

The runs differed from each other with respect to the acquisition method, labeled *continuous* or *sparse*, and the behavioral paradigm, labeled *rest* or *task*. Together, this gave 4 possible combinations, for each of which two runs were performed (see Fig. 1). In the continuous runs, images were acquired without interruption (200 volumes; TR 2.0 s); in the sparse runs (Hall et al., 1999), functional acquisitions were alternated with 8.0-s periods of scanner inactivity (40 volumes; TR 10.0 s). In the rest runs, subjects were instructed to remain awake and lie still with their eyes open, but no task was imposed and no stimuli were delivered; in the task runs, subjects performed an auditory memory task that involved the presentation of sound stimuli through MR-compatible electrodynamic headphones (MR Confon GmbH, Magdeburg, Germany) (Baumgart et al., 1998).

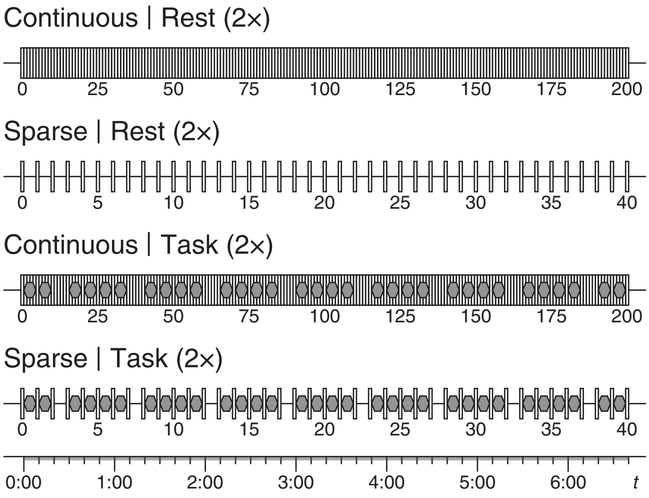

Fig. 1. Experimental design. Four different types of functional runs were acquired. Each 2-s EPI acquisition is illustrated in the form of a vertical open bar; each 8-s sound stimulus is represented as a shaded hexagon. Two acquisition methods (continuous and sparse) were combined with two task paradigms (rest and task). During continuous scanning, 200 image volumes were acquired without interruption. In contrast, the 40 sparse acquisitions were separated by periods of scanner inactivity. Additional preparation scans (labeled '0' in the figure) were executed but were not analyzed. The rest runs did not include any task performance or stimulus presentation. The task runs included the presentation of a series of diverse sound fragments, including one silent interval among every five consecutive fragments. Subjects were instructed to memorize the fragments, and their recollection was tested after the fMRI session. The sound stimuli were presented during the periods of scanner inactivity for the sparse runs, and at corresponding moments (while the scanner was active) for the continuous runs. Each type of run was repeated twice per subject, and corresponding runs were pair-wise concatenated for further analysis.