NeuroImage 146 (2017) 171–187

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/neuroimage

Robustness and dynamicity of functional networks in phantom sound

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ARTICLE INFO

Article history:
Received 14 December 2015
Accepted 14 April 2016
Available online 18 April 2016

Keywords:
Tinnitus
EEG
Multimodal
Rich-club
Damage-modeling

ABSTRACT

Phantom sound perception is the perception of a sound in the absence of a corresponding external sound source. It is a common symptom for which no treatment exists. Gaining a better understanding of its pathophysiology by applying network science might help in identifying targets in the brain for neuromodulatory approaches to treat this elusive symptom. Brain networks are commonly organized as functional modules which have a densely connected core network coupled to a communally-organized peripheral network. The core network is called the rich club network and the peripheral network is divided into the feeder and local networks. In current study, we investigate the effects of virtual lesions on the endogenous dynamics, complexity and robustness of the remaining brain. It is hypothesized that depending on whether nodes is functionally central to the network or not, the robustness and dynamics of the network change when a lesion in introduced. We therefore investigate the effect of introducing a virtual focal lesion randomly to different nodes is in the tinnitus network and contrast it to the effect of specifically targeting the nodes of the rich-club, feeder and local nodes in patients experiencing a phantom sound (i.e. tinnitus). The tinnitus and control networks were computed from the source-localized EEG of 311 tinnitus patients and 256 control subjects. The results of the current study indicate that both the tinnitus and control networks are robust to the attack on random and rich club nodes, but are drastically modified when attacked from the periphery, especially while targeting the feeder hubs. In both the tinnitus and control networks, feeder nodes were found to have a higher betweenness centrality value than the rich club nodes. This shows that the feeders have a larger influence on the information transmission through the brain than the rich club nodes, by transferring information from the peripheral communities to the core. Further, evidence for the theoretical model of a multimodal tinnitus network is also presented showing that the tinnitus network is divided into individual, separable modules each possibly encoding a different aspect of tinnitus. The current study alludes to the concept that the efficient modification of the tinnitus network is theoretically possible by disconnecting the individual communities from the core of the pathological network.

1. Introduction

Application of network connectomics has spanned a vast majority of domains such as social (Duncan J. Watts, 1999), computer (Strogatz, 2001), protein (Wuchty, 2001) and brain networks (Danielle Smith Bassett and Bullmore, 2006). According to graph theory, these networks are structured into a "small-world" topology (Duncan J. Watts, 1999; D. J. Watts and Strogatz, 1998) within which individual nodes connect to each other and a small proportion of nodes, called hubs, facilitate long-distance connectivity (D. S. Bassett et al., 2008). This has become a widely accepted model for complex systems because it accounts for an economic balance between network efficiency and the structural cost of wiring the system (Sophie Achard and Bullmore, 2007; Danielle Smith Bassett and Bullmore, 2006; Bullmore and Sporns, 2012; Strogatz, 2001; Duncan J. Watts, 1999). The robustness of such functional networks has been investigated in a number of complex systems (Albert et al., 2000; Doyle et al., 2005), including biological networks (Alstott et al., 2009; Jeong et al., 2001). From a network perspective, changes in brain dynamics as a result of acute injuries such as trauma, tumor, or stroke, as well as chronic or degenerative disturbances, correspond to node and edge deletions in the brain connectome (Alstott et al., 2009). Conversely, in the current study, we investigate the effects of theoretically inducing focal lesions (by removing a set of spatially localized nodes) on the endogenous dynamics, complexity and robustness of the remaining brain.

Networks can be further described as having a community structure (Flake et al., 2002; Fortunato, 2010), a core-periphery structure (Holme, 2005; Rombach et al., 2014) or a combination of the two (Yang and Leskovec, 2014). Community structures have been

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http://dx.doi.org/10.1016/j.neuroimage.2016.04.033

Table 1
Characteristics of tinnitus patients.

Ear	
Unilateral	114
Bilateral	197
Tone	
Pure tone	118
Noise Like	193
TQ	
Mean	39.37
SD	17.59
Tinnitus frequency (Hz)	
Mean	5143
SD	3183
Tinnitus loudness (dB SL)	
Mean	7.85
SD	8.78

characterized to typically consist of densely populated, specialized modules that are functionally integrated through sparse inter-modular connections (Fortunato, 2010). On the other hand, a core-periphery based structure is cemented on a foundational core network which branches outwardly into a diffuse peripheral network (Rombach et al., 2014). However, the core may or may not be central to the network as a whole (Holme, 2005). A combination of community and core-periphery structures has been shown to materialize into a multimodal network with overlapping communities (Yang and Leskovec, 2014). This results in a network having a densely connected core which is coupled to an organized peripheral network. Such a structure has been extensively studied in brain networks as the "rich-club" connectome (Bullmore and Sporns, 2012; M. P. van den Heuvel and Sporns, 2011). The peripheral network in a "rich-club" connectome further consists of a feeder network which provides direct input to the rich club nodes and a local network consisting of connections between non rich-club nodes (M. P. van den Heuvel and Sporns, 2011; Martijn P. van den Heuvel and Sporns, 2013). The feeder nodes along with the rich club nodes are responsible for inter-modular connections and the local network is responsible for intra-modular connections.

The current study aims to investigate the robustness of functional brain networks to virtual focal lesions and presents empirical evidence for a multimodal network organization that is disorder specific. This involves the removal of nodes at random or in association with a certain network parameter (nodes with high betweenness centrality or belonging to the rich club, feeder or local networks). We focus on the cortical differences in resting-state, eyes-closed, source localized EEG between tinnitus patients and healthy controls. Tinnitus or phantom sound is the perception of a sound in the absence of a corresponding external auditory stimulus. It is a common symptom for which no treatment exists (Langguth et al., 2013). Gaining a better understanding of its pathophysiology by applying network science might provide an empirical tool for identifying targets in the brain for effective neuromodulation of this elusive symptom. Tinnitus is a complex functional disorder which is characterized by multiple components such as pitch, loudness, associated mood and distress changes, laterality, type (noise-like, pure tone) etc. (De Ridder et al.,

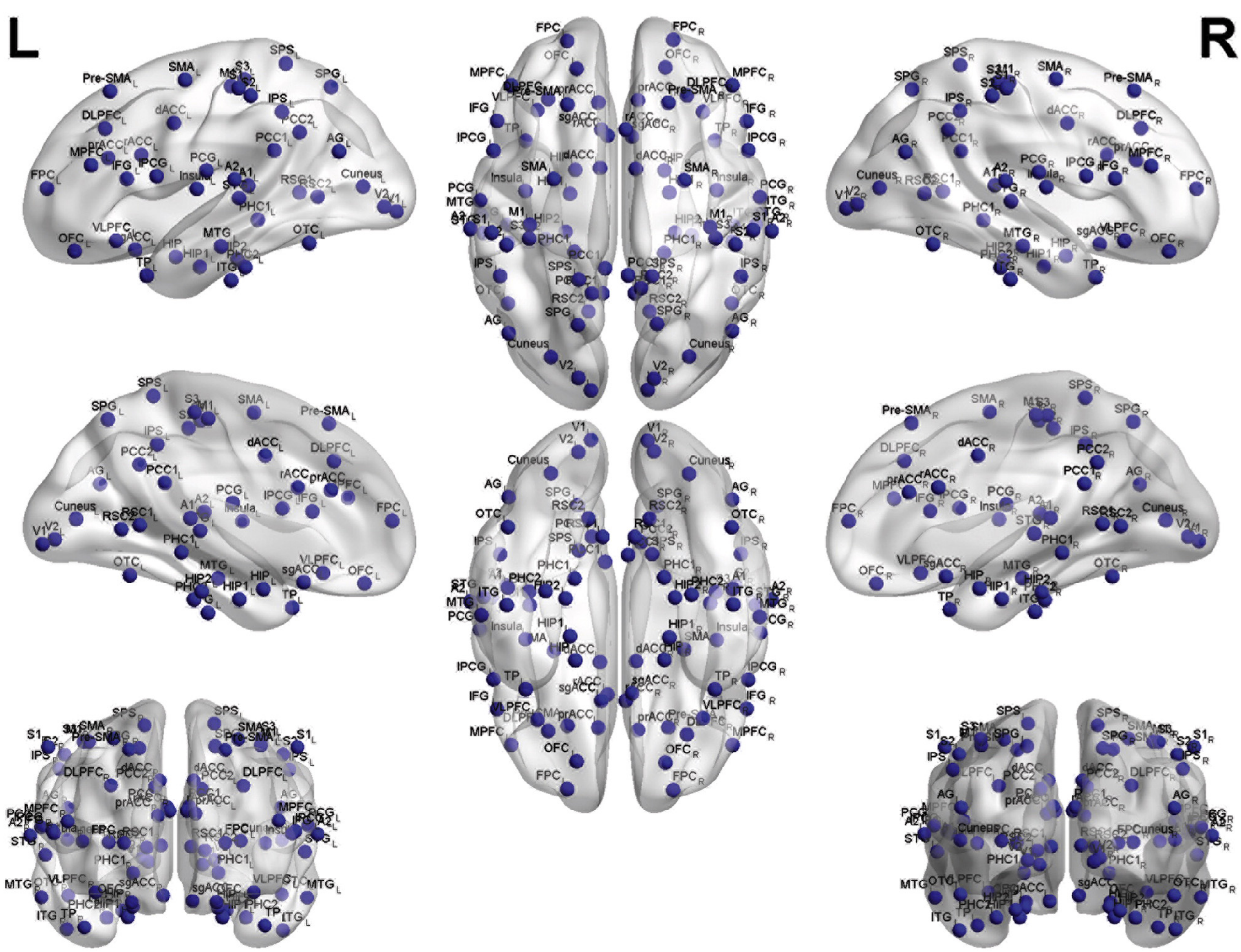

Fig. 1. All the Brodmann areas included in the study.