Neuropsychologia 113 (2018) 29–42

Contents lists available at ScienceDirect

Neuropsychologia

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

Task-induced deactivation in diverse brain systems correlates with interindividual differences in distinct autonomic indices☆

Vittorio Iacovella[a,*], Luca Faes[b,c], Uri Hasson[a,d]

[a] Center for Mind/Brain Sciences, The University of Trento, Trento, Italy
[b] BIOtech, Department of Industrial Engineering, University of Trento, Trento, Italy
[c] IRCS PAT-FBK Trento, Italy
[d] Center for Practical Wisdom, The University of Chicago, Chicago, USA

ARTICLE INFO

Keywords:
ANS
Deactivation
Arithmetic
Interindividual differences

ABSTRACT

Neuroimaging research has shown that different cognitive tasks induce relatively specific activation patterns, as well as less task-specific deactivation patterns. Here we examined whether individual differences in Autonomic Nervous System (ANS) activity during task performance correlate with the magnitude of task-induced deactivation. In an fMRI study, participants performed a continuous mental arithmetic task in a task/rest block design, while undergoing combined fMRI and heart/respiration rate acquisitions using photoplethysmograph and respiration belt. As expected, task performance increased heart-rate and reduced the RMSSD, a cardiac index related to vagal tone. Across participants, higher heart rate during task was linked to increased activation in fronto-parietal regions, as well as to stronger deactivation in ventromedial prefrontal regions. Respiration frequency during task was associated with similar patterns, but in different regions than those identified for heart-rate. Finally, in a large set of regions, almost exclusively limited to the Default Mode Network, lower RMSSD was associated with greater deactivation, and furthermore, the vast majority of these regions were task-deactivated at the group level. Together, our findings show that inter-individual differences in ANS activity are strongly linked to task-induced deactivation. Importantly, our findings suggest that deactivation is a multifaceted construct potentially linked to ANS control, because distinct ANS measures correlate with deactivation in different regions. We discuss the implications for current theories of cortical control of the ANS and for accounts of deactivation, with particular reference to studies documenting a "failure to deactivate" in multiple clinical states.

1. Introduction

Understanding the computations that different brain regions perform during task performance continues being one of the main undertakings of modern cognitive neuroscience. In investigating this issue, multiple studies show that task-evoked changes are not limited to brain networks strictly associated with task-related information processing. Specifically, engagement in different tasks (e.g., language, attention, memory) impacts activity and connectivity (e.g., Fransson and Marrelec, 2008; McKiernan et al., 2006, 2003) of a "default mode" network (DMN) that is thought to mediate spontaneous, task-independent computations such as mind wandering (Mason et al., 2007).

Another way by which tasks can perturb brain activity is by modulating brain networks involved in Autonomic Nervous System (ANS) monitoring and regulation, which are often found to be distinct from the DMN in terms of topology and function (as we review below). The ANS is strongly impacted by tasks that present arousing stimuli or that specifically employ emotional stressors (e.g., Thayer et al., 2012, 2009). However, the ANS is also perturbed by affectively neutral tasks such as mental arithmetic or Stroop tasks (for review, see Beissner et al., 2013). Such perturbations have been linked to fluctuations in task performance (see Critchley and Garfinkel, 2015, for review).

Our general aim in the current study was to establish how individual-differences in ANS activity relate, if at all, to BOLD deactivation during an affectively neutral task. Specifically, we examined whether there are brain networks where the magnitude of task-induced deactivation is associated with interindividual differences (IID) in ANS reactivity during performance of a simple continuous mental arithmetic task. Our study addresses two fundamental issues concerning the relation between IID in ANS activity and task-related deactivation (as well

☆ This research was supported by European Research Council Starting Grant ERC-STG #263318 NeuroInt to U.H.
* Corresponding author.
E-mail address: vittorio.iacovella@unitn.it (V. Iacovella).

https://doi.org/10.1016/j.neuropsychologia.2018.03.005
Received 5 October 2017; Received in revised form 30 January 2018; Accepted 3 March 2018
Available online 09 March 2018
0028-3932/ Published by Elsevier Ltd.

as task-related activation). First, as we review below, few prior studies have specifically taken on a systematic examination of whether IID in ANS activity are related to task-induced activation or deactivation. And second, those studies that examined this question had relied on a single autonomic measure. Consequently, whether the magnitude of task-related deactivation in different brain systems is associated with different ANS indices, is a topic simply not addressed to date.

Interestingly, there exist marked IID in both ANS reactivity and task-induced deactivation, suggesting these may load on shared factors. Inter-individual differences in ANS reactivity are not only prevalent within non-clinical participant groups (Goldberger et al., 2001; Karemaker and Wesseling, 2008), but also vary with age (Pfeifer et al., 1983), and with personality features during development (Beauchaine, 2001). Altered ANS function is also associated with clinical states such as autism (Hirstein et al., 2001) or depression (Carney et al., 2005). In tandem, IID in task-related (de)activation have also been reported, and these have been associated with similar factors to those that impact ANS. For instance, IID in activation/deactivation have been linked to stress level (Soares et al., 2013), age (Persson et al., 2007) meditation (Lutz, Brefczynski-Lewis, Johnstone, Davidson, 2008) or clinical states such as autism and schizophrenia that have been linked to a "failure to deactivate" during simple cognitive tasks (e.g., Kennedy et al., 2006; Landin-Romero et al., 2015). Interestingly, IID in task-related activation/deactivation also correlate with differences in resting-state (baseline) fluctuation levels (Zou et al., 2013), which in turn are also linked to IID in ANS activity (Jennings et al., 2016). We therefore hypothesized that IID in ANS reactivity, as measured in a normal non-clinical group of participants, could be related to the extent of task-induced activation/deactivation.

Several studies have reviewed the brain systems involved in regulation of the ANS, particularly from the perspective of the psychology of emotion, or the involvement of ANS in interpersonal interactions (for reviews and meta-analyses, see, Beissner et al., 2013; Thayer et al., 2012). The relation between ANS function and brain activity during simple cognitive tasks has received less investigation. Beissner et al. (2013) reported a meta-analysis of neuroimaging studies that used motor, emotional or cognitive stressors. The meta-analysis showed that affective, motor and cognitive tasks produce different relations between ANS activity and brain activity (see also Thayer et al., 2012, for a meta-analysis focusing on parasympathetic correlates). Particularly relevant for our current inquiry, Beissner et al. showed that during cognitive-task stressors, parasympathetic responses were linked to the left amygdala and right anterior insula. Sympathetic activity was linked to mid-cingulate cortex, left anterior insula, left secondary somatosensory cortex, vmPFC, subgenual ACC, left superior parietal lobule, left supramarginal gyrus, and left amygdala.

We note that the relation between IID in ANS responses and task-related activation has been largely ignored in many prior neuroimaging studies, specifically because typical analyses collapse across these differences. As such, the bulk of prior work has focused on identifying brain regions where activity covaries with ANS fluctuations at the group level, and so between-participant differences were modeled as random effects. This was achieved, for example, by including time-series of ANS fluctuations as an explanatory variable (regressor) in single-subject BOLD-fMRI regression models (Critchley et al., 2003, 2005; Evans et al., 2009; Napadow et al., 2008), using block-mean ANS measures as parametric modulators in block designs (Fechir et al., 2010) or establishing ANS/PET-rCBF correlations on the single-participant level (Gianaros et al., 2004; Lane et al., 2009). Crucially, in all these analyses, the single-participant regression coefficients were used in second-level analyses to identify ANS-related activity at the group level, and IID were not quantified.

Furthermore, some neuroimaging studies that did report BOLD correlates of IID in ANS, limited their analysis to brain areas strongly implicated in the experimental task studied. To illustrate, Matthews et al. (2004) identified clusters sensitive to congruence in a Stroop task, and only within those did they evaluate correlations between heart-rate variability (HRV) and response levels to congruent and incongruent trials. This approach may be less sensitive to identifying activity-correlates of IID in ANS, as brain areas that are most strongly task-activated, or most strongly discriminative of two conditions at the group level may be those least impacted by arousal. In another fMRI study (Muehlhan et al., 2013) the authors examined IID in sympathetic responses as measured by salivary alpha amylase (sAA) while participants responded to validly- or invalidly-cued targets. The authors identified brain regions that satisfied two criteria: task-induced activity changes (either activation or deactivation) and significant BOLD/sAA correlations. Perhaps due to the motor-component of this task, the task-active regions that also showed correlations with sAA were not ones typically associated with the ANS. However, the authors identified several task-deactive regions including the left precuneus, angular gyrus bilaterally, vmPFC and left middle frontal gyrus. In all these regions, higher arousal was associated with greater deactivation. This and prior work (Nagai et al., 2004; Wong et al., 2007) suggests that increased arousal is associated with greater disturbance of the 'default' process mediated by these regions.

To our knowledge, two studies have specifically treated the issue of IID in ANS as the focus of investigation. Wager et al. (2009) found that during responses to social threat, rostral and pregenual ACC showed a positive correlation between heart rate reactivity and task-induced activation. The right orbitofrontal cortex was deactivated by the task and showed an inverse correlation, so that heart rate reactivity was associated with greater deactivation. Importantly, in both regions, rapid BOLD fluctuations tracked fluctuations in heart rate, indicating that deactivated regions may track ANS fluctuations on a fine temporal scale. Gianaros et al. (2012) examined IID in beat-to-beat blood pressure and interbeat intervals (measurements obtained in mock fMRI scanner). They correlated a mental effort index of the task (effect size for *difficult_task - easy_task*) with IID in ANS reactivity. Across participants, stronger effect sizes were associated with stronger suppression of baroreflex sensitivity [BRS], an ANS index reflecting the short-term homeostatic control of blood pressure. This was found across the cingulate cortex but also in the insula and midbrain. The study considered however a single physiological index (BRS), which is also difficult to measure within a scanning environment thus reducing its applicability for everyday neuroimaging studies.

To summarize, there is limited understanding of how task-induced deactivation is related to IID in different autonomic measures. This holds particularly for emotionally-neutral cognitive tasks and for ANS-related metrics that can be established from typical cardiac and respiratory in-scanner recordings. To examine this issue, we established the magnitude of task-induced activation (or deactivation), and evaluated it against several ANS measures. We selected measures that differentially load on sympathetic and parasympathetic sources, and that can be derived from physiological signals collected concurrently with task performance in an fMRI scanner. Importantly, because we wanted to know whether IID correlations between ANS and task-induced effects are mainly found in areas linked to task-induced deactivation, our analytic approach departed from prior work: we first identified areas where task-related activity correlated with IID in ANS measures, and then determined whether these areas were associated with task-related activation or deactivation.

We employed a silent mental arithmetic (MA) subtraction task, in absence of any exogenous behavioral performance. The task was conducted in a blocked manner to allow modeling task-induced changes in activity. Then, as a first step, we used a group-level voxel-wise robust-regression approach to identify brain areas where IID in ANS indices correlated with task-induced signal change. These regions then constituted functional regions of interest (fROIS). In a last step, for each fROI, we conducted group-level tests to determine whether it showed statistically significant task-induced activation or deactivation. In this way, our approach did not limit the Brain/ANS investigation to regions