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# Phasic alerting effects on visual processing speed are associated with intrinsic functional connectivity in the cingulo-opercular network

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ABSTRACT

Phasic alertness refers to short-lived increases in the brain's "state of readiness", and thus to optimized performance following warning cues. Parametric modelling of whole report task performance based on the computational theory of visual attention (TVA) has demonstrated that visual processing speed is increased in such cue compared to no-cue conditions. Furthermore, with respect to the underlying neural mechanisms, individual visual processing speed has been related to intrinsic functional connectivity (iFC) within the cingulo-opercular network, suggesting that this network's iFC is relevant for the tonic maintenance of an appropriate readiness or alertness state. In the present study, we asked whether iFC in the cingulo-opercular network is also related to the individual ability to actively profit from warning cues, i.e. to the degree of phasic alerting. We obtained resting-state functional magnetic resonance imaging (rs-fMRI) data from 32 healthy young participants and combined an independent component analysis of rs-fMRI time courses and dual regression approach to determine iFC in the cingulo-opercular network. In a separate behavioural testing session, we parametrically assessed the effects of auditory phasic alerting cues on visual processing speed in a TVA-based whole report paradigm. A voxel-wise multiple regression revealed that higher individual phasic alerting effects on visual processing speed were significantly associated with lower iFC in the cingulo-opercular network, with a peak in the left superior orbital gyrus. As phasic alertness was neither related to iFC in other attention-relevant, auditory, or visual networks nor associated with any inter-network connectivity pattern, the results suggest that the individual profit in visual processing speed gained from phasic alerting is primarily associated with iFC in the cingulo-opercular network.

## 1. Introduction

External warning cues induce short-lived changes in the brain's "state of readiness" defined as phasic alertness (Robertson et al., 1998; Sturm and Willmes, 2001). Numerous studies have demonstrated faster reaction times in conditions with warning cues compared to control conditions (e.g. Coull et al., 2001; Fan et al., 2005; Posner, 1978; Posner and Boies, 1971). While these phasic alerting benefits were initially suggested to reflect speeded preparation and execution of motor reactions (Posner, 1978; Sturm and Willmes, 2001), a fMRI study reported higher BOLD activity in perceptual areas, i.e. bilateral extrastriate regions and left precuneus, in target detection task trials preceded by alerting cues (without any spatial information) compared to no-cue trials (Thiel et al., 2004). In line with this finding, more recent studies have demonstrated benefits in preceding visual perceptual processes induced by visual (Matthias et al., 2010) and auditory warning cues (Haupt et al., 2018; Petersen et al., 2017). More precisely, these benefits pertain to an increase in the speed of visual information uptake.

Verbal report paradigms of briefly presented letter arrays combined with modelling based on the computational Theory of Visual Attention

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*Abbreviations:* TVA, Theory of Visual Attention of Bundesen; iFC, intrinsic functional connectivity; rs-fMRI, resting-state functional magnetic resonance imaging; vSTM, visual short term memory.

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(TVA) provide a parameter-based approach to measure attentional functions, particularly visual processing speed and – importantly for our study – changes in visual processing speed following alerting cues (Bundesen, 1990). TVA is closely related to the biased competition account (e.g. Desimone and Duncan, 1995) and implies parallel processing of several visual objects that are competing for selection into a visual short term memory (vSTM) store with limited capacity. The probability that an object gets selected before the store is filled is proportional to its processing rate. The processing rate at which the categorization "object $x$ belongs to category $i$" is made is the product of the strength of sensory evidence that "$x$ belongs to category $i$" and the visual bias of the observer towards category $i$.

$$v(x, i) = \eta(x, i)\, \beta_i \quad (1)$$

Critically for the present study, the extended model of components of visual bias suggests the visual bias to be computed as a product of three factors:

$$\beta_i = A\, p_i\, u_i \quad (2)$$

$A$ reflects the level of alertness, $p_i$ is the subjective prior probability of a certain feature, e.g. temporal expectancy (Vangkilde et al., 2013, 2012), and $u_i$ refers to the utility or subjective importance of this feature (Bundesen et al., 2015). Accordingly, an increase of phasic alertness will lead to a proportional increase in the observer's bias towards an object and, thus, to a proportional increase in the processing rate of the object. The sum of the processing rates of all objects present in the visual display is defined as the overall visual processing speed $C$ (in elements per second) of a given observer (Habekost et al., 2013). By definition, all items in a whole report share the same expectancy and subjective importance. An increase in the observer's alertness $A$ induced by alerting cues will lead to a proportional increase in parameter $C$ (Bundesen et al., 2015). Thus, by comparing visual processing speed in conditions with and without warning cues, the individual phasic alerting effect on visual information uptake can be measured.

It is assumed that TVA parameters depict relatively stable characteristics of a participant's attentional capability across different situations (Finke et al., 2005). We suggest that, comparable to other attentional parameters modelled based on TVA, an individual's ability to prepare for upcoming stimuli and optimize performance based on phasic alerting cues also depicts such a relatively stable capability or "trait-like" parameter. It is to be expected that the ability to optimize performance based on such cues varies among individuals. Accordingly, standard neuropsychological diagnostic procedures for the assessment of attention, e.g. Test Battery for Attentional Performance (TAP; Zimmermann and Fimm, 2002), include tasks measuring an individual's ability to profit from phasic alerting cues and relate this ability to the respective age norm. Therefore, stable inter-individual variations of alerting effects can be deployed to investigate the neural basis of this active perception mechanism, i.e. linking phasic alerting effects to intrinsic brain networks as they are both stable, "trait-like" parameters.

In previous TVA-based studies, individual visual attention functions have been linked to large-scale functional brain networks derived from resting-state functional magnetic resonance imaging (fMRI) data (Ruiz-Rizzo et al., 2019, 2018). In resting-state fMRI, ongoing fluctuations of the blood oxygen level dependent (BOLD) signal with a frequency around 0.01–0.1 Hz can be measured and analyzed (Fox and Raichle, 2007). Spatial patterns of coherent, i.e. correlated, BOLD fluctuations over time (termed intrinsic functional connectivity, iFC) constitute intrinsic brain networks. These intrinsic brain networks are stable on an intra- (Zuo et al., 2010) and inter-subject (Damoiseaux et al., 2006; De Luca et al., 2006) level. They are also highly consistent across species and states of consciousness, ranging from sleep to rest and task performance (Buckner et al., 2013; Fox and Raichle, 2007; Raichle, 2011). The spatial outlines of the networks largely correspond to underlying structural connectivity networks identified by diffusion tensor imaging (Hagmann et al., 2008; Honey et al., 2009, 2007). However, direct structural connections between two areas are not a prerequisite for intrinsic functional connections between them (Damoiseaux and Greicius, 2009; Raichle, 2011). The ongoing slow fluctuations in fMRI BOLD signal show cross-frequency correlations with slow cortical power ($<$4 Hz) and gamma band-limited power (50–100 Hz) measured with intracranial recordings (He et al., 2008) as well as with alpha, beta, and theta frequencies measured in magnetoencephalography (MEG) (Hipp et al., 2012; for a review see Engel et al., 2013). It is proposed that the phases of lower frequencies modulate the amplitudes of higher frequencies in an upward progression across the frequency spectrum (He et al., 2010). Such cross-frequency coupling is suggested to be of fundamental importance in the functional organization of the brain's activity (Raichle, 2011). Most importantly for the present study, iFC can be associated with (e.g. Visintin et al., 2015) and even predict (e.g. Rosenberg et al., 2018, 2017, 2015) individuals' behavioural performance in attention tasks. Connectome-based predictive modelling (Shen et al., 2017) can predict alerting scores assessed in the Attention Network Test (ANT), i.e. a more pronounced speeding of reaction times in central-cue compared to no-cue trials, from resting-state functional connectivity (Rosenberg et al., 2018). This finding provides evidence that connectivity patterns observed at rest, i.e. without any online administered task, contain a separable signature of the brain's ability to prepare for upcoming events (Rosenberg et al., 2018).

In particular, individual visual processing speed $C$ values have been found to be related to iFC in the cingulo-opercular network (Ruiz-Rizzo et al., 2019, 2018), a brain network comprising regions such as the anterior prefrontal cortex, anterior insula, frontal operculum, dorsal anterior cingulate cortex, medial superior frontal cortex, and thalamus (Dosenbach et al., 2008). Importantly, iFC in this network, which has also been referred to as "salience network" (e.g. Seeley et al., 2007) or "ventral attention network" (e.g. Yeo et al., 2011), has been shown to be related to the intrinsic maintenance of an appropriate level of alertness during task performance (Coste and Kleinschmidt, 2016; Sadaghiani and D'Esposito, 2015) and has also been linked to indices of alertness, such as spontaneous upper alpha band oscillations (Sadaghiani et al., 2010) as well as spontaneous pupil dilations (Schneider et al., 2016). These findings are in line with a previous review of positron emission tomography (PET) and fMRI studies suggesting that phasic alertness is associated with activations of attention networks comprising bilateral frontal, parietal, and brainstem structures (Sturm and Willmes, 2001).

The present study sets out to investigate the neural correlate of active enhancements of visual processing speed. More specifically, we test whether the individual degree of phasic alerting effects, as measured by cue-induced changes in visual processing speed $C$ in an offline administered TVA-based whole report paradigm, is linked to the individual iFC in the cingulo-opercular network acquired during resting-state fMRI. We hypothesize that phasic alerting effects are selectively associated with iFC in the cingulo-opercular network. In order to assure the specificity of the interrelation, we carry out control analyses to assess whether the phasic alerting effect, as predicted, is selectively associated with iFC in the cingulo-opercular network or whether it is rather globally linked to iFC within multiple intrinsic brain networks. To address this, we analyse associations of the phasic alerting effect with iFC in other attention-relevant, auditory, and visual networks. As we are employing a visual attention task with auditory cues, we additionally explore the inter-network connectivity between the cingulo-opercular network and the mentioned other intrinsic brain networks to gain insight into the question whether the functional connectivity between those networks is also associated with phasic alerting effects.

## 2. Material and methods

### 2.1. Participants

Thirty-six healthy adults at the age of 18–35 years participated in the present study. Two participants were excluded because of extreme visual processing speed *C* estimates that were not representative for the group (>2 SDs from the group mean). One further participant did not participate in the MRI session and one had to be excluded because of low functional imaging data quality. Therefore, the final sample consisted of 32 participants (see Table 1). All participants reported normal or corrected-to-normal vision. The study was reviewed and approved by the ethics committees of the Department of Psychology of the Ludwig-Maximilians-Universität München and the Klinikum rechts der Isar of the Technical University Munich. All participants gave informed consent, and were either reimbursed for their participation or received course credit. The data and code used in the present study are available upon direct request and the data sharing complies with the institutional ethics approval.

The acquisition of the resting-state fMRI (approx. 1 h) and the offline TVA-based behavioural assessment (approx. 1 h) took place on two different days. Participants also completed the Edinburgh Handedness Inventory (Oldfield, 1971) and a multiple choice German vocabulary test measuring crystallized intelligence, "Mehrfachwahl-Wortschatz-Intelligenztest" (MWTB; Lehrl et al., 1995) (see Table 1).

## 2.2. *Behavioural assessment*

The behavioural data presented here has already been reported in a previous publication (Haupt et al., 2018).

### 2.2.1. *TVA-based whole report paradigm*

The details of the applied TVA-based whole report procedure have been explained elsewhere (Haupt et al., 2018). All possible trial sequences can be seen in Fig. 1a. In summary, each trial consisted of six equidistant target letters (each 1.2 cm high, 1.0 cm wide) that were randomly chosen from a set of 23 letters (ABCDEFGHJKLMNOPRSTUVWXZ; every letter appeared only once per trial) and were presented on an imaginary circle (0.9 cm diameter) around the central fixation point. Participants were instructed to maintain central fixation and verbally report all letters recognized with "fair certainty" without any importance of speed or order. After entering all reported letters on the keyboard, the experimenter started the next trial with a button press. This variability in trial length was necessary to allow for the participants' unspeeded verbal report. A scale presenting the individual's accuracy rating based on all reported letters succeeded every test block. Participants were asked to maintain an accuracy level between 70% and 90% with a deviating score leading to adapted instructions for the next test block. If the participants' accuracy rating exceeded 90%, they were asked to also name letters that they believed to have recognized without complete certainty. If participants were less than 70% accurate, they were instructed to only report letters recognized with high certainty even if that meant that they would report less letters overall. For each participant, five individual target exposure durations were determined in a pretest phase and later used for all experimental blocks. The experiment consisted of 8 blocks with 84 trials each, resulting in an overall duration of one to one and a half hours. Throughout the experiment, target displays presented with the 5 adjusted exposure durations were followed by masks (max.1.8 × 1.8 cm, 500 ms). In addition, two exposure durations were also presented without a subsequent mask. Due to iconic memory buffering in unmasked compared to masked trials, this resulted in seven effective exposure durations (Sperling, 1960).

**Table 1**
Demographics and visual processing speed (*C*) estimates of all participants.

| Variable | All Participants | p value |
|---|---|---|
| | N = 32 | |
| mean age (SD) | 26.6 (4.7) | – |
| sex (female/male) | 20/12 | – |
| handedness (right/left) | 27/5 | – |
| mean education in years (SD) | 12.6 (0.9) | – |
| MWTB score (SD) | 28.6 (4.6) | – |
| Number of days between behavioural session and rs-fMRI session | 240.1 (294.7) | – |
| *C* in cue condition/no-cue condition | 34.7 (11.6)/30.7 (9.3) | <.001 |

*Note.* SD: standard deviation; handedness: assessed by Edinburgh Handedness Inventory; MWTB: Mehrfachwahl-Wortschatz-Intelligenztest, maximum score = 37 points.

### 2.2.2. *Alerting conditions*

In the alerting-cue condition, the target display was preceded by an auditory cue (80 dB, randomly chosen with a frequency of either 500 Hz or 900 Hz) that contained no spatial information about the upcoming target location but was deployed to enhance participants' phasic alertness for a few hundred milliseconds. During the presentation of the tone (200 ms), the screen remained blank with only the fixation point being visible. Comparably, in the no-cue condition, participants saw a blank screen for 200 ms without any tone being presented. The cue target onset asynchrony (CTOA) had an average of 260 ms and was jittered around this value in steps of ± 20 ms, 40 ms and 60 ms leading to an overall range of 200–320 ms. For each trial, one CTOA was randomly drawn from the described CTOA range. As the whole behavioural experiment contained two different CTOA ranges (Haupt et al., 2018) but the present study only analyzes data from one CTOA range, 336 experimental trials are included in the estimation of TVA parameters and subsequent statistical analyses. In the present study, we only include data from the long CTOA range as participants showed consistent phasic alerting effects on visual processing speed when a longer CTOA was employed. In the shorter CTOA, high-performing individuals demonstrated ceiling effects of visual processing speed, derogating phasic alerting effects (Haupt et al., 2018).

### 2.2.3. *Estimation of TVA parameters*

The whole report task allows for the estimation of visual processing speed *C*, vSTM storage capacity *K*, and visual perceptual threshold *t0*. While the estimation of all parameters is needed for retrieving valid estimates of visual processing speed *C*, parameter *K* and *t0* are of no specific interest in the current study (note that alertness cues were repeatedly shown to predominantly affect visual processing speed, see Haupt et al., 2018; Matthias et al., 2010; Petersen et al., 2017). Furthermore, the variable of interest in the present study ($C_{\text{cue}}$) is not significantly correlated with $K_{\text{cue}}$, $K_{\text{no-cue}}$, $t0_{\text{cue}}$, and $t0_{\text{no-cue}}$ (all $\tau < 0.206$, all $p > .098$, all $BF < 0.854$). Hence, the present study sets out to address the specific relationship between visual processing speed *C* and iFC in the cingulo-opercular network.

For detailed underlying estimation algorithms please refer to Kyllingsbaek (2006). The mathematically modeled exponential growth function is relating the report accuracy (mean number of reported items) to the underlying effective exposure duration. Accordingly, the function's intersection with the x-axis defines the visual perceptual threshold *t0*. The slope of the function at this intersection indicates the visual processing speed *C* (total rate of information uptake in objects per second). Furthermore, the asymptote denotes the maximum number of represented object defined as vSTM storage capacity *K* (see Fig. 1b).

## 2.3. *Resting-state fMRI*

### 2.3.1. *Imaging data acquisition*

Imaging data were acquired on a 3T MR scanner (Philips Ingenia,

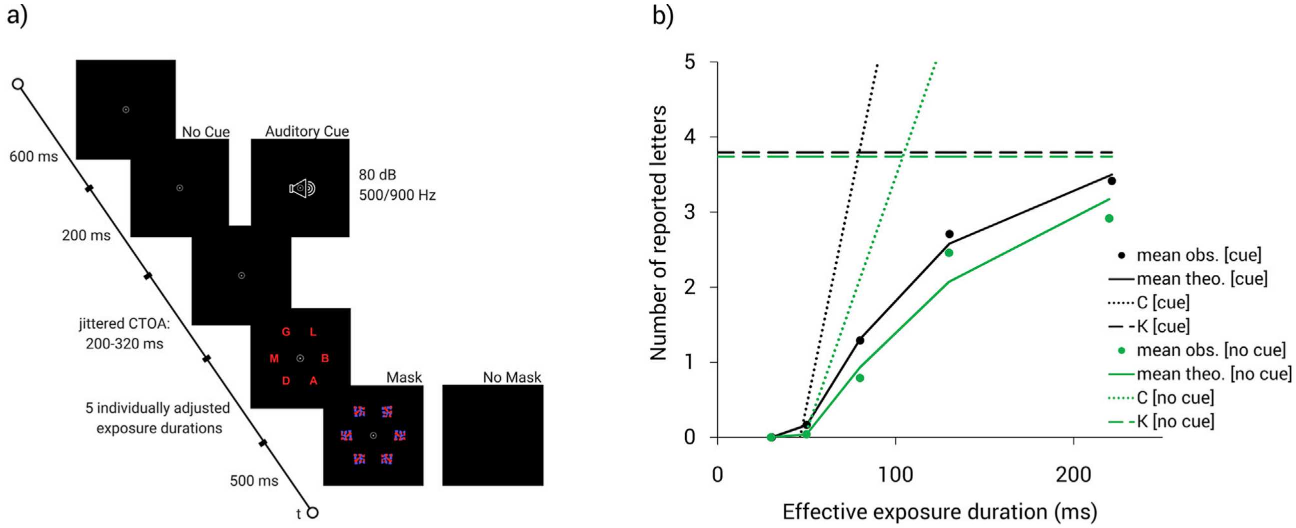

**Fig. 1.** Trial sequence in whole report paradigm (a) and whole report performance for a representative younger participant (b). The graph (b) contains a comparison between the cue and no-cue condition. The observed values are displayed as single data points (mean obs.). Solid curves represent the best theoretical fit from the TVA to the observations (mean theo.). The vSTM storage capacity $K$ is defined as the asymptote of the function and is marked by a dashed line. The visual perceptual threshold $t0$ is defined by the origin of the function (coordinate: t0,0). Visual processing speed $C$ is defined as the slope of the function in $t0$ and is represented by a dotted line.

Netherlands) using a 32-channel SENSE head coil. Small cushions stabilized participants' heads in the head coil to reduce head motion. Earplugs and headphones reduced scanner noise. Functional data acquisition lasted for 12.5 min and participants were instructed to keep their eyes closed, intend to stay awake, and to refrain from performing any cognitive or motor activity, i.e. be at rest, throughout the whole sequence. The functional data set consisting of 600 volumes was acquired by multi-band echo-planar imaging (EPI; Preibisch et al., 2015) with a multi-band SENSE acceleration factor of 2 (TR = 1250 ms; TE = 30 ms; phase encoding in anterior-posterior direction; flip angle = 70°; field of view (FOV) = 192 mm$^2$; matrix size = 64 × 64, 40 slices with 3 mm thickness and an inter-slice gap of 0.3 mm; reconstructed voxel size = 3 mm × 3 mm × 3.29 mm). Structural data were obtained by a T1-weighted magnetization-prepared rapid-acquisition gradient echo (MPRAGE) sequence (TR = 9 ms; TE = 4 ms; flip angle = 8°; FOV = 240 mm$^2$; matrix = 240 × 240, 170 sagital slices; reconstructed isotropic voxel size = 1 mm).

### 2.3.2. Imaging data preprocessing

The resting-state fMRI data were preprocessed in MATLAB (R2017b, version 9.3.0.713579; The Mathworks Inc.) using SPM 12 version 6225 (https://www.fil.ion.ucl.ac.uk/spm/software/spm12/) and the Data Processing Assistant for Resting-State fMRI toolbox version 2.3 (DPARSF; Chao-Gan and Yu-Feng, 2010). After removing the first five functional volumes of every data set to account for T1 saturation effects, slice timing and head motion correction were performed by calling SPM functions. Slice timing correction is often omitted when imaging data are acquired by multi-band echo-planar imaging as, in this case, the repetition times are shorter than in conventional acquisition methods. However, up to our knowledge, it is still an open question whether repetition times in multiband image acquisition are actually short enough to completely omit slice time correction (Parker et al., 2017). Therefore, in general, slice timing correction depicts an advisable preprocessing step for functional imaging data (Sladky et al., 2011). None of the participants had to be excluded due to excessive head motion by the criterion of cumulative translation or rotation of 3 mm or 3° or due to more than 15% frame-wise displacements >0.5 mm (Power et al., 2012). All images were manually reoriented to the AC-PC axis. The functional images were normalized into Montreal Neurological Institute (MNI) space with a 2-mm isotropic voxel size by unified segmentation to the structural image (Ashburner and Friston, 2005). DPARSF integrates the three underlying procedures - coregistration, segmentation (grey matter, white matter, cerebrospinal fluid) and writing normalization parameters - into one processing step. The normalized images were smoothed using a 4 mm full-width-at-half-maximum (FWHM) Gaussian kernel. Additionally, band-pass filtering (0.01–0.1 Hz) was performed and the effects of nuisance covariates (whole-brain signal, white matter, cerebrospinal fluid, and scrubbing regressors for derivative 12 head motion parameters) were removed.

### 2.3.3. Independent component analysis and dual regression analyses

After preprocessing the functional data, we conducted a probabilistic Independent Component Analysis (ICA) in FSL (version 5.0.9) using the MELODIC command-line program version 3.14 (Beckmann and Smith, 2004; Smith et al., 2004). We specified 20 independent components aiming at decomposing the data into larger “primary networks” and avoiding to split up the data into relatively smaller “subnetworks” following the approach of Smith et al. (2009). The ICA decomposed each time × space matrix into pairs of time courses and spatial maps on the group level. Subsequently, these files were used as input and a dual regression was employed in order to estimate spatial maps and time courses for each participant (Beckmann et al., 2009; Filippini et al., 2009). The dual regression approach allows to quantify the functional connectivity of each voxel with each spatial map while controlling for all other spatial maps within each participant (Smith et al., 2014). Most importantly, we chose this approach as dual regression analysis is excelling in detecting inter-individual variability in functional connectivity compared to seed-based functional connectivity analysis (Smith et al., 2014). In a first step, the group-average spatial map was regressed into the individual participants' time × space matrices, resulting in a participant-specific time series. In a second step, the group-average time series was regressed into the same matrices, yielding 20 participant-specific spatial maps, i.e. one per independent spatial map on the group-level. The individual spatial maps contain Z-scores of every voxel within the according map. These Z-scores indicate the similarity of a particular voxel's time course to the time course of the respective component on the group-level while controlling for all other components. Therefore, the voxel-wise Z-scores were used as input for statistical tests to analyse whether the given component derived Z-scores do relate to behavioural variables. Importantly, the results of the statistical analyses are solely related to the specific output of the ICA, i.e. independent components. These components represent intrinsic brain networks, but the precise brain regions included may vary, so that results of statistical analyses might manifest in brain areas that belong to the independent component, but are not typically included in a certain brain network (Smith et al., 2014). In a last step, the randomize permutation-testing tool (5000 permutations, $p = .05$) within the FSL framework yielded group spatial maps (Beckmann et al., 2009; Filippini et al., 2009).

In order to identify typical intrinsic brain networks with our ICA-dual regression approach, we performed a spatial cross-correlation of our 20 independent components with intrinsic brain network templates derived from Allen et al. (2011). Accordingly, we identified the component with the strongest correlation coefficient with the "salience network" (component IC55, $r = 0.44$) of Allen et al. (2011) as the cingulo-opercular network in the present study.

## 2.4. Statistical analyses

### 2.4.1. Analyses of phasic alerting effects on visual processing speed

Visual processing speed $C$ values in the cue and no-cue conditions did not follow a normal distribution. Therefore, the data were analysed with a nonparametric Wilcoxon signed-rank test. In addition, the Bayesian equivalent of a paired samples *t*-test (Rouder et al., 2009) was conducted using JASP version 0.8.5.1 (JASP Team, 2018). The Bayes factor (BF) is a measure for the ratio of the likelihoods of two theories. Hence, the Bayes factor allows for a quantification of the evidence for the null hypothesis and the alternative, experimental hypothesis. If $BF_{10}$ is greater than 3 the present data substantially support the alternative hypothesis while values smaller than 1/3 substantially favor the null hypothesis (Dienes, 2011; Wagenmakers et al., 2011).

### 2.4.2. Analyses of phasic alerting effects on visual processing speed and iFC in the cingulo-opercular network

The individual spatial maps resulting from the described second step of the dual regression served as input for the intra-network analyses conducted in SPM12 (http://www.fil.ion.ucl.ac.uk/spm/software/spm12/) and additional nonparametric analyses using the Statistical NonParametric Mapping toolbox (SnPM13, http://warwick.ac.uk/snpm). According to Hayes and Rockwood (2017), modelling post-scores or difference scores using pre-scores as covariates yields more precise estimates of change than pure differences scores because it accounts for regression to the mean. Thus, we performed a voxel-wise multiple regression of visual processing speed $C$ in the cue condition on iFC in the cingulo-opercular network while controlling for visual processing in the no-cue condition ($p < .05$ FWE corrected for multiple comparisons at the cluster level, voxel-wise height threshold $p < .001$).

To further confirm the robustness and validity of the association between phasic alerting effects on visual processing speed and iFC in the cingulo-opercular network, we ran additional multiple regressions using alternative indices of the individual alertness cueing benefit as regressor of interest, i.e. absolute difference ($C_{\text{cue}} - C_{\text{no-cue}}$), relative cueing effect ($(C_{\text{cue}} - C_{\text{no-cue}})/(C_{\text{no-cue}})$), and the standardized cueing effect ($(C_{\text{cue}} - C_{\text{no-cue}})/(C_{\text{cue}} + C_{\text{no-cue}})$). Furthermore, we assessed whether the choice of a specific covariate influences the outcome of the multiple regression by keeping the regressor of interest constant (absolute difference) while adding either $C$ in the no-cue condition or overall $C$ (averaged over cue and no-cue trials) as a covariate of no interest.

In all voxel-wise analyses, we added age, education, and sex as planned covariates. The variable of interest ($C_{\text{cue}}$) is not significantly correlated with any of these control variables ($-0.149 < \text{all } \tau < 0.058$, all $p > .241$, all $BF_{10} < 0.458$). However, differences in sex, age, and cognitive ability (possibly related to years of education) are suggested to be reflected in distinct connectivity patterns and power spectra within multiple resting state networks (e.g. Allen et al., 2011; Smith et al., 2014; Zhang et al., 2016). To ensure that our results are not driven by the added covariates, we also repeated the voxel-wise multiple regression of visual processing speed $C$ in the cue condition on iFC in the cingulo-opercular network without age, sex, and education as covariates (only controlling for visual processing speed in the no-cue condition).

In addition, we repeated our analysis twice to account for the influence of head motion and time between the behavioural and fMRI session. Firstly, we controlled for the influence of head motion by re-running the mentioned multiple regression with mean volume-to-volume head motion, i.e. frame-wise displacement, as an additional covariate. We chose the measure by Jenkinson et al. (2002) as it considers voxel-wise differences in its derivation (Yan et al., 2013). We also directly correlated frame-wise displacement with the behavioural variable of interest. Secondly, we added days between sessions as a covariate to the voxel-wise multiple regression. Again, we also correlated the variable days between sessions with the behavioural variable of interest.

### 2.4.3. Control analyses regarding the specificity of the association between phasic alerting effects and iFC in the cingulo-opercular network

In order to address the specificity of the relationship between phasic alerting effects on visual processing speed $C$ and the cingulo-opercular network, we additionally performed control analyses in other attention-related, auditory, and visual networks. We identified them by visual inspection and cross-correlation ($0.37 < \text{all } r < 0.48$) with templates by Allen et al. (2011) (IC71, IC52, IC60, IC17, IC39 and IC46). Firstly, we chose to control for alerting associations with iFC in the executive control network (IC71) as this network has been reported to be co-activated with the cingulo-opercular network during fMRI tasks but its iFC is dissociable from iFC within the cingulo-opercular network (Seeley et al., 2007). Seeley et al. (2007) suggest that iFC in the executive control network is associated with higher order cognitive processes such as working memory and sustained attention. Secondly, we analyzed the association of phasic alerting effects with iFC in left (IC52) and right (IC60) lateralized fronto-parietal networks as these intrinsic brain networks comprise the main alerting-related structures reported by a review of PET and fMRI task studies (Sturm and Willmes, 2001). Thirdly, we tested for a significant relation between alerting effects and iFC in the auditory network (IC17) as our behavioural task contains an auditory cue. Lastly, we repeated the analyses in two visual networks (IC39 and IC46) as we are employing a behavioural task consisting of visual stimuli.

For all mentioned networks, we repeated the analyses using a nonparametric regression approach with 10000 permutations in order to yield an empirical cumulative distribution function of the statistic under the null hypothesis and to control for type I errors.

### 2.4.4. Analyses of inter-network connectivity between the cingulo-opercular network and other attention-relevant and sensory networks

Finally, we investigated whether the cingulo-opercular network's inter-network functional connectivity with attention-related, auditory, or visual networks is also significantly associated with phasic alerting effects. We addressed this question by entering the individual time courses of the mentioned intrinsic brain networks (yielded by the first step of dual regression) into an inter-network analysis (using custom

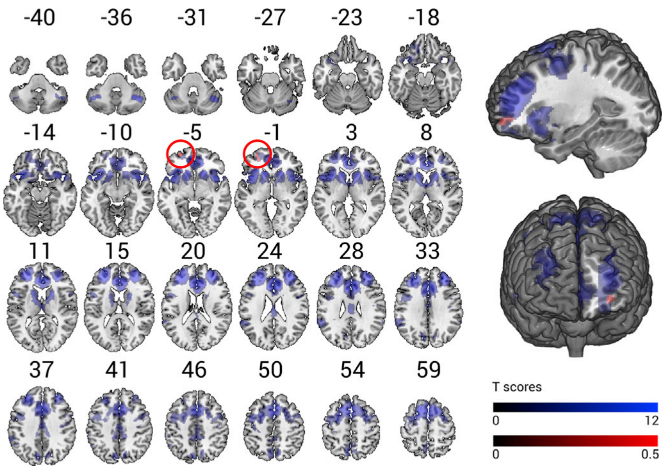

**Fig. 2.** Statistical Parametric Mapping of voxel-wise multiple regression of visual processing speed in alerting cue condition (red) on iFC in cingulo-opercular network (blue). The results are obtained by independent component analysis of resting-state fMRI data and are overlaid onto standard anatomical MNI152 templates using the software MRIcroGL (available at: https://www.mccauslandcenter.sc.edu/mricrogl/source); slice numbers in transverse plane are indicated. The results of the multiple regression are controlled for visual processing speed in the no-cue condition, age, sex, and education ($p < .05$ FWE corrected at cluster level).

code written in MATLAB; also see Ruiz-Rizzo et al., 2018). We correlated the time course of the cingulo-opercular network with the ones derived from the other six independent components of interest per participant. Subsequently, we performed Fisher r-to-Z transformation and partial correlation analyses to test whether the inter-network connectivity of the cingulo-opercular network with any other network was significantly correlated with visual processing speed $C$ in the cue condition when controlling for visual processing speed $C$ in the no-cue condition.

## 3. Results

### 3.1. Phasic alerting effects on visual processing speed

The Wilcoxon signed-rank test was employed to compare visual processing speed in the cue ($M = 34.7$, $SD = 11.6$, letters per second) and no-cue ($M = 30.7$, $SD = 9.3$, letters per second) condition. The test yields a significant difference between both conditions ($Z = 338$, $p < .001$, $r_b = 0.697$), i.e. visual processing speed $C$ in the cue condition was significantly higher than in the no-cue condition, indicating a successful phasic alerting effect of the auditory warning cue. The Bayesian analysis confirms the significant alerting effect on visual processing speed $C$. The Bayes Factor of $BF_{10} = 43.17$ very strongly supports the alternative hypothesis of the visual processing speed estimates in both alerting conditions being significantly different from each other.

### 3.2. Relation of phasic alerting effects on visual processing speed and iFC in the cingulo-opercular network

The cingulo-opercular network encompasses the cerebellum, amygdala, insula, basal ganglia, thalamus, paracingulate gyrus, anterior cingulate cortex, orbital gyrus and frontal gyri (inferior, middle and superior) (see Fig. 2).

The voxel-wise multiple regression analysis yielded a significant relationship between the individual degree of phasic alerting effects on visual processing speed $C$ and iFC in the cingulo-opercular network. Specifically, when controlling for age, sex, education, and also for baseline visual processing speed $C$ values in the no-cue condition, higher individual alerting effects on visual processing speed were significantly associated with lower individual iFC in the cingulo-opercular network, with a peak in the left superior orbital gyrus (MNI coordinates in mm: [-26 46–2], cluster size: 66 voxels, $T = 4.91$, $p = .003$, FWE corrected for multiple comparisons at the cluster level with applied voxel-wise height threshold of $p = .001$) (see Fig. 2).

To confirm the robustness and validity of the association between phasic alerting effects on $C$ and iFC in the cingulo-opercular network, we conducted the same analysis with the absolute difference ($C$ in no-cue trials as covariate), absolute difference (overall $C$, averaged over cue and no-cue trials, as covariate), relative cueing effect, and the standardized cueing effect as regressor of interest. All analyses yielded the same significant peak within the cingulo-opercular network (see Supplements Table 1). This indicates that the association of phasic alerting effects with the iFC in the cingulo-opercular network is robust regardless of which specific measure of phasic alerting effects on $C$ and the specific baseline $C$ that were chosen as the regressor of interest and covariate.

In addition, we repeated the voxel-wise multiple regression of visual processing speed $C$ in the cue condition on iFC in the cingulo-opercular network without age, sex, and education as covariates (only controlling for visual processing in the no-cue condition). The analysis yields a significant association of a higher alerting effect on visual processing speed with lower iFC in the cingulo-opercular network in a comparable, only slightly extended, cluster (MNI coordinates in mm: [-30 56–4], cluster size: 85 voxels, $T = 4.77$, $p = .001$).

This result is also stable when either frame-wise displacement (MNI coordinates in mm: [-26 46–2], cluster size: 65 voxels, $T = 4.78$, $p = .003$) or days between sessions (MNI coordinates in mm: [-28 60–6], cluster size: 76 voxels, $T = 5.11$, $p = .001$) are added as a covariate to the described voxel-wise multiple regression with sex, age, and education as covariates. Further, we controlled for head motion and time between sessions by calculating nonparametric correlation of $C_{cue}$ with frame-wise displacement ($\tau = 0.137$, $p = .270$, $BF_{10} = 0.410$) and days between sessions ($\tau = -0.218$, $p = .080$, $BF_{10} = 1.002$).

These additional analyses show that the results of the voxel-wise multiple regression of visual processing speed $C$ in the cue condition on iFC in the cingulo-opercular network remain constant whether or not the planned covariates are added. Furthermore, the results demonstrate that estimates of head motion, i.e. frame-wise displacement, and time between sessions are neither correlated with visual processing speed, nor change the results of the voxel-wise multiple regression when added as an additional covariate. Taken together, these findings suggest that none of the covariates are driving the observed brain-behaviour relationship.

### 3.3. Control analyses regarding the specificity of the association between phasic alerting effects and iFC in the cingulo-opercular network

To determine whether phasic alerting effects on $C$ are specifically linked to iFC in the cingulo-opercular network, we controlled for phasic alerting associations with iFC in other networks. The parametric and non-parametric multiple regression analyses yielded no significant association of the individual degree of phasic alerting effects on visual processing speed with iFC in the executive control network, left and right fronto-parietal networks, auditory network, as well as visual networks (all $p > .05$). As in the main analyses, all control analyses included age, sex, education and visual processing speed $C$ values in the no-cue condition as covariates. Importantly, the result in favour of the null hypothesis in the executive control network, left and right fronto-parietal networks, auditory network, as well as visual networks demonstrate that phasic alerting effects on C are not significantly associated with iFC in these networks. The non-parametric analysis confirmed that the null results were not due to violations of the normality assumption. However, we cannot directly compare the behaviour-iFC relationship in the cingulo-opercular network with the behaviour-iFC relationships in the control networks as we used a voxel-wise analysis approach.[2] Considering this limitation, we can summarize that the iFC of the assessed auditory, visual, and attention-related networks is not significantly associated with phasic alerting, suggesting a primary association of phasic alerting effects on C and iFC in the cingulo-opercular network.

### *3.4. Inter-network connectivity between the cingulo-opercular network and other attention-relevant and sensory networks*

In order to trace whether the inter-network connectivity of the cingulo-opercular network is also significantly associated with phasic alerting effects on $C$, we entered the above mentioned attention-related, auditory, and visual networks into an inter-network analysis. The analysis yielded a significant positive correlation of the cingulo-opercular network with the right fronto-parietal network (IC60) as well as significant negative correlations with the auditory network (IC17), and both visual networks (IC39, IC46). The correlations of the cingulo-opercular network with the left fronto-parietal network (IC52) and the executive control network (IC71) were not significant (see Supplements Fig. 1).

Importantly, partial correlation analyses revealed that none of the described significant inter-network correlations were, in turn, significantly correlated with visual processing speed $C$ in the cue condition when controlling for $C$ in the no-cue condition ($-0.254 \leq$ all $r \leq 0.206$, all $p \geq 180$). These results indicate that the decisive link between the phasic alerting effect on visual processing speed $C$ and the cingulo-opercular network is its intra-network iFC and not its inter-network connectivity with other attention-relevant, auditory, or visual networks.

## 4. Discussion

When provided with warning signals, observers can temporarily increase their arousal state. In particular, they can speed up their rate of visual information uptake by recruiting additional attentional processing resources (Haupt et al., 2018; Matthias et al., 2010; Petersen et al., 2017). Such active optimization is decisive for efficient behaviour in situations where fast visual perception is essential for quick and accurate responses, such as traffic, sports, and social communication scenarios.

The present study set out to identify the underlying neural network mechanisms of this relevant phasic alerting effect by relating individual differences in the degree of phasic alerting effects on visual processing speed $C$ measured in an offline administerd TVA-based paradigm to those in intrinsic functional connectivity (iFC) in the cingulo-opercular network (acquired by resting-state fMRI). We chose iFC in the cingulo-opercular network as it was previously suggested to play a significant role in alertness (Coste and Kleinschmidt, 2016; Sadaghiani et al., 2010; Sadaghiani and D'Esposito, 2015; Schneider et al., 2016) and visual processing speed (Ruiz-Rizzo et al., 2019, 2018). Furthermore, the cingulo-opercular network comprises some of the structures that have been suggested to be particularly relevant for the phasic component of alertness induced by warning cues, i.e. bilateral frontal, and brainstem structures (Sturm and Willmes, 2001).

In our study, a voxel-wise multiple regression analysis revealed that, indeed, more pronounced cueing effects on visual processing speed were significantly related to iFC in the cingulo-opercular network. The relationship was inversed, i.e. phasic alertness effects were negatively associated with iFC in the cingulo-opercular network. The result proved to be robust regardless of which alerting score (score in cue condition controlled for score in no-cue condition, absolute difference, relative difference, or standardized cueing effect) was used as dependent variable in the analysis. This result underlines that the association between phasic alerting effects on visual processing and iFC in the cingulo-opercular network does not solely rely on the chosen definition of the alerting effect but can be generalised across measures of phasic alerting effects. We also addressed the specificity of the association between phasic alerting and iFC in the cingulo-opercular network by employing control analyses regarding the intra-network connectivity in other relevant attention-related and sensory networks. IFC in the executive control network, left and right fronto-parietal networks, auditory, and visual networks were not significantly related to phasic alerting effects. Additional inter-network connectivity analyses of the cingulo-opercular network and other attention-related, auditory, and visual networks indicated that inter-network connectivity could not account for inter-individual differences in phasic alerting. In sum, the results indicate that phasic alerting effects on visual processing speed are robustly and primarily associated with iFC in the cingulo-opercular network with a peak in the left superior orbital gyrus.

According to the extended TVA model of visual bias, an increase in the perceptual bias parameter $\beta$ leads to a proportional increase in visual processing speed $C$ in a whole report paradigm. The perceptual bias $\beta$ is a product of three factors including alertness $A$ (Bundesen et al., 2015). Hence, if the other two factors are held constant, the increase in $C$ is proportional to the increase in alertness (induced by the auditory cues). In the present study, the estimated average processing speed $C$ is 34.7 items per second in the cue condition, and 30.7 items per second in the no-cue condition. This translates to a phasic increase in the alertness parameter $A$ of around 13%, i.e. an alertness factor of 1.13. The neural interpretation of TVA (NTVA; Bundesen et al., 2005) suggests that the perceptual decision bias parameter influences the level of activation in neurons induced by a visual display. Hence, the theory suggests that enhancing phasic alertness by cues increases the activation levels of cells. It has been suggested that slow fluctuations in BOLD signal, measuring the brain's default activity pattern, reflect slow propagating waves providing sub-threshold depolarization to individual neurons, resulting in an increased spiking probability of those neurons (Matsui et al., 2016; Sanchez-Vives et al., 2017; Wu et al., 2008). In a recent study, Schwalm et al. (2017) suggested that local calcium events do underlie these slow waves and are directly linked to a global cortical fMRI BOLD signal. Therefore, it seems plausible that spontaneous fluctuations of cortical excitability on the basis of propagating waves influence brain's “state of readiness” regarding the processing of incoming information. Our data suggest that the individual spatial patterns of coherent fluctuations among regions of the cingulo-opercular network are related to the

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[2] For every individual, the Dual Regression succeeding the Independent Component Analysis yields one spatial map per component (relating to a specific intrinsic brain network) containing Z-scores of every voxel. These Z-scores indicate the similarity of the time course of a particular voxel to the time course of the respective component on the group-level. Accordingly, we do not obtain one meaningful value representing the intrinsic functional connectivity (iFC) in a given component (intrinsic brain network) per participant. Therefore, we cannot calculate a correlation between one behavioural score and one iFC score in a certain network for every participant. Rather, we employ a voxel-wise multiple regression approach, i.e. for every participant we quantify the degree to which the behavioural score (while controlling for covariates) is related to the Z-score (of a given voxel) separately for every voxel that is part of the network. We either compare the observed differences in behaviour-iFC relationships with the null distribution of differences (permutation tests in SnPM) or the t-distribution (in SPM). We then (1) apply a voxel-wise height threshold ($p < .001$) and (2) correct for multiple comparisons at the cluster level (FWE correction, $p < .05$). Clusters of significant associations between the behavioural score and the Z-scores of the comprised voxels are interpreted as a proof-of-principle of a significant association between the behavioural variable of interest and iFC in the according intrinsic brain network. Accordingly, we would be able to compare iFC-behaviour relationships across networks if clusters in other networks would have surpassed the cluster-level significance threshold. In this case, for every network, we could have calculated the correlation between the behavioural score and Z-scores of voxels in the significant cluster, and could have, later on, statistically compared those correlation scores across networks. However, we do not find significant clusters in any network but the cingulo-opercular network. In summary, we cannot directly compare behaviour-iFC relationships between networks as, based on our voxel-wise analysis approach, we neither have one meaningful value representing iFC on the network-level, nor do we have one cluster-based iFC value for each network.

individual excitability, i.e. to the relevant ability to arouse the visual processing system in order to increase the readiness to perceive information in a fast manner, specifically in situations that require speeded processing.

The results of the present study complement previous findings demonstrating that resting-state functional connectivity patterns can predict alerting scores measured in the Attention Network Test (ANT; Rosenberg et al., 2018). Rosenberg et al. (2018) demonstrated that intra-temporal, occipital-parietal, and temporal-motor connections significantly predicted higher alerting scores. However, specific whole-brain functional connectivity networks cannot be directly compared to the network findings in the present study. Firstly, while the present study employs a voxel-wise multiple regression preceded by an ICA and Dual regression approach, Rosenberg et al. (2018) use a 268 node functional brain atlas as the basis of network definition. Accordingly, the behaviour is related to the time courses of each of these nodes, which in turn are defined as the averaged time courses of all voxels in each node. Secondly, both tasks yield distinct measures of alerting (for a comparison of the ANT and TVA-based assessment also see: Habekost et al., 2014). The ANT measures phasic alerting effects as the difference between reaction time in a no-cue and a cue condition. The association between temporal-motor connections and high alerting scores might thus reflect an increase in the readiness to prepare and execute motor reactions (Rosenberg et al., 2018). As, in contrast, the TVA-based measure of alertness is a pure measure of visual attention, i.e. perceptual effects of alerting cues, we do not see such a relationship. However, both studies provide crucial evidence that functional connectivity patterns observed in resting-state fMRI, i.e. when no behavioural task is administered during fMRI acquisition, can be linked to individuals' ability to prepare for upcoming stimuli, i.e. phasic alertness.

Importantly, our result should not be interpreted as the peak region, i.e. left superior orbital gyrus, being particularly “responsible” for phasic alerting effects. As we employed a voxel-wise approach, the iFC values of the significant voxels in the left superior orbital gyrus (Z scores) are in principle relative values. This means that they can only be interpreted in relation to iFC of other voxels within in the brain. Regarding the cingulo-opercular network, we can, therefore, solely predicate that the inverse relationship between phasic alerting effects on visual processing speed and iFC in the cingulo-opercular network was best represented in the left superior orbital gyrus. Such representation of the phasic alertness iFC relationship in the left hemisphere is principally in line with former studies reporting a left-hemispheric involvement during tasks employing phasic alerting cues (Coull et al., 2001) as compared to tonic alertness conditions (Sturm and Willmes, 2001). However, the results do not imply a specific role of the left superior orbital gyrus for phasic alertness.

Interestingly, the present study reveals a negative association between phasic alerting effects on visual processing speed and iFC in the cingulo-opercular network. This finding can be reconciled with results from a previous resting-state fMRI study (Ruiz-Rizzo et al., 2018). Ruiz-Rizzo et al. (2018) demonstrated that young, healthy participants with higher (vs. lower) visual processing speed $C$ as obtained in a standard TVA-based whole report task without alerting cues, were characterized by lower iFC in the cingulo-opercular network as assessed in a separate rs-fMRI session. Visual processing speed in such uncued conditions is assumed to reflect an individual's level of intrinsic (tonic) alertness (Matthias et al., 2010). Taken together, the results of these two studies might imply that participants with a low iFC in the cingulo-opercular network have a relatively efficient processing system. This could lead to both relatively high processing speed $C$ in paradigms that require the intrinsic maintenance of arousal, i.e. tonic alertness, and a relatively efficient active utilization of exogenous cues to improve their visual processing speed, i.e. phasic alertness. Our finding relates to a task-evoked fMRI study by Sadaghiani and D'Esposito (2015). The authors found that participants with a high overall accuracy in a pitch discrimination paradigm show lower BOLD activity in the cingulo-opercular network compared to low performing individuals. The authors suggested that, for these high performers, the task might have imposed lower demands on their alerting system (Sadaghiani and D'Esposito, 2015). Thus, the results from the present study might suggest that participants with a rather efficient alertness system might not be forced to recruit the cingulo-opercular network to the same extent as less efficient and lower performing participants. Potentially, this pattern could already be reflected in iFC patterns measured in a resting-state condition, in which the only task for the participants is to keep an appropriate arousal level in order not to fall asleep while they are not engaged in any particular task.

We suggest individual effects of phasic alertness on visual processing speed to have a trait-like character. Such a relatively constant parameter could potentially be associated with intra-network and, importantly, also inter-network connectivity between different intrinsic brain networks. For example, it was previously demonstrated that visual processing speed in uncued conditions showed both, a negative association with intra-network connectivity in the cingulo-opercular network and a positive one with inter-network connectivity between the cingulo-opercular and right fronto-parietal network (Ruiz-Rizzo et al., 2018). While in the present study, we did not find such significant associations for phasic alerting effects with inter-network connectivity, this does not necessarily indicate that coupling to other intrinsic brain networks is not relevant. Potentially, effective connectivity measures constitute a promising approach to reveal relevant directed, i.e. effective, connectivity patterns between brain networks or within the same network (Mottaghy et al., 2006; Périn et al., 2010; Riedl et al., 2016) that might not be depictable with iFC measures. Importantly, such interactions of the cingulo-opercular network with other networks or brain stem structures could potentially also explain a negative relationship of behaviour and intra-network connectivity as recently suggested by Ruiz-Rizzo et al. (2018). A candidate structure relevant for phasic alerting effects is the locus coeruleus, which was shown to be functionally connected to some nodes of the cingulo-opercular network in healthy younger (Zhang et al., 2016) and older (Serra et al., 2018) participants during resting state. Accordingly, a TVA-based study demonstrated that increases in visual processing following phasic alerting cues were accompanied by increases in pupil dilation (Petersen et al., 2017), a measure known to correlate with BOLD activity in the locus coeruleus (Murphy et al., 2014). Therefore, phasic alerting effects on visual processing speed could be associated with iFC of the locus coeruleus and brain structures forming the cingulo-opercular network. The present study could not address this question as we did not acquire physiological data to account for physiological noise in the brainstem originating from adjacent arteries and cerebrospinal fluid filled spaces. Future studies will be needed to shed light on this question.

Beyond the specific questions derived from the negative association of phasic alerting effects and iFC in the cingulo-opercular network, the present findings also potentially have several overarching implications for future studies. First, the question arises how the brain regions of the cingulo-opercular network interact with visual areas in order to accelerate the uptake of visual information. It has been suggested that brain regions within the cingulo-opercular network, especially the insula, play a decisive role in phasic alertness, i.e. mediate sensory alertness by heightening the readiness to respond to stimuli in sensory cortices (Sterzer and Kleinschmidt, 2010). It also seems plausible that specific intrinsic brain networks are connected with each other. In the present study, we could not find associations of phasic alerting effects on visual processing speed with inter-network connectivity of the cingulo-opercular network and visual networks. This might indicate that iFC as a measure is not sensitive enough to capture uni- or bidirectional communication between brain areas. Methods such as metabolic connectivity mapping could aid in revealing effective connectivity patterns (Riedl et al., 2016). Furthermore, studies using brain stimulation techniques constitute a promising approach to address the directionality of connections between brain areas within specific networks. Finally, a recent establishment of a TVA-based mouse paradigm opens the avenue to experimentally study the brain system functions underlying alertness effects on visual processing speed (Fitzpatrick et al., 2017).

Secondly, establishing a neural correlate of phasic alerting in the optimally functioning brain systems of young healthy persons allows to test whether such an association is altered in populations that are known to show changes in visual processing speed, phasic alertness functions, and/or iFC. For example, iFC in the cingulo-opercular network is prone to age-related changes (He et al., 2014; Onoda et al., 2012; Ruiz-Rizzo et al., 2019). It has, however, been shown that phasic alerting effects on visual processing speed are preserved in healthy aging (Haupt et al., 2018), although older participants' phasic alerting benefits might be more vulnerable to paradigm changes than the ones found in young participants (Wiegand et al., 2017). Thus, the question arises whether phasic alerting effects in healthy aging individuals rely on the same or differing underlying spatial patterns of iFC. Furthermore, visual processing speed is significantly reduced in pathological aging, i.e. in patients suffering from mild cognitive impairment and Alzheimer's disease (Bublak et al., 2011; Neitzel et al., 2016; Ruiz-Rizzo et al., 2017), psychiatric disorders (Gögler et al., 2017b, 2017a; McAvinue et al., 2015), and in diverse neurological patient populations (for a review on clinical TVA-based studies, see Habekost, 2015). Improved knowledge on the residual degree to which phasic alerting can improve visual processing speed in these patient populations and the relationship to iFC changes in the cingulo-opercular network could pave the way for new treatment options.

Thirdly, establishing a link for the degree of short-term enhancement of visual processing speed also opens the avenue to assess whether the individual degree of more long-term excitability might be related to iFC in the cingulo-opercular network. Future studies might address the question whether iFC in the cingulo-opercular network allows for individualized prediction of the individual response to phasic alertness training (e.g. Tennstedt and Unverzagt, 2014), and might, therefore, be used for tailoring interventions for persons with alertness dysfunctions.

## 5. Conclusions

In summary, the present study demonstrates that phasic alerting effects on visual processing speed are primarily associated with iFC in the cingulo-opercular network.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.neuroimage.2019.04.019.

## Disclosure statement

The authors have no actual or potential conflicts of interest.

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