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Cortical and subcortical contributions to interference resolution and inhibition – An fMRI ALE meta-analysis

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ABSTRACT

Interacting with our environment requires the selection of appropriate responses and the inhibition of others. Such effortful inhibition is achieved by a number of interference resolution and global inhibition processes. This meta-analysis including 57 studies and 73 contrasts revisits the overlap and differences in brain areas supporting interference resolution and global inhibition in cortical and subcortical brain areas. Activation likelihood estimation was used to discern the brain regions subserving each type of cognitive control. Individual contrast analysis revealed a common activation of the bilateral insula and supplementary motor areas. Subtraction analyses demonstrated the voxel-wise differences in recruitment in a number of areas including the precuneus in the interference tasks and the frontal pole and dorsal striatum in the inhibition tasks. Our results display a surprising lack of subcortical involvement within these types of cognitive control, a finding that is likely to reflect a systematic gap in the field of functional neuroimaging.

1. Introduction

Cognitive control as a whole describes an array of processes required for optimal and adjustable human behaviour and decision-making (Aron, 2007; Botvinick et al., 2001). Under this umbrella of cognitive control are two associated but inherently distinct mechanisms that aid in supporting the ability of goal-directed behaviour; interference resolution and global inhibition (Nigg, 2000). These concepts have drawn the attention of psychologists since the late 19th century (Bergstrom, 1894), where the terms were initially used interchangeably but due to clinical psychology and neuroscience results it became apparent that these are two related but functionally diverse phenomena (Nee et al., 2007). In general, global inhibition is defined as the global dampening of an already initiated or no longer relevant action (Aron, 2007). Interference resolution is considered a more selective inhibition process, where task-irrelevant stimuli and goal-irrelevant responses must be dampened but relevant responses maintained (Nigg, 2000). In the past, both these types of inhibition processes have been largely studied independently. Global inhibition has commonly been investigated using the Stop-Signal task (Logan et al., 1984) or the Go/No-Go task (Donders, 1969), which overlap in terms of global inhibition but differ with respect to the underlying proactive or reactive mechanism. Interference resolution has been largely studied through the use of the Eriksen-Flanker task (Eriksen and Eriksen, 1974), Stroop task (Stroop, 1935), Simon task (Simon and Rudell, 1967) and multi-source interference task (Bush et al., 2003).

Generally agreed upon theories of the biological architecture underlying these types of cognitive control rest on the involvement of both the cortex and subcortex (Albin et al., 1989; Aron et al., 2016; Nambu et al., 2002; Neumann et al., 2018; Wiecki and Frank, 2013). It has long been hinted that a cortico-striatal loop modulates the capacity of interference resolution (Mink, 1996; Utter and Basso, 2008), and there is evidence that the STN plays a key role in the net-inhibition of inappropriate movements (Beauregard and Lévesque, 2006; Frank, 2006; Forstmann et al., 2012; Guitart-Masip et al., 2011; Keuken et al., 2015; Wessel et al., 2019). Recent studies have found evidence that the fronto-striatal network supports the ability to selectively inhibit such movements (Schmidt et al., 2018, 2020), in line with theories suggesting that the basal ganglia modulate these cortical pathways to some extent (Alexander et al., 1986; Mink, 1996; Utter and Basso, 2008). Another source of evidence for the involvement of subcortical areas in interference resolution and global inhibition comes from intracranial recordings studies. There is a sizable and growing body of literature showing the involvement of the STN in stopping ongoing action as a result of surprising events as well as mediates post-error slowing in subsequent trials.
Yet, time and time again, these deeper regions are often underrepresented in fMRI studies and as a result the meta-analytical evidence for subcortical involvement in interference resolution is limited (e.g., Chen et al., 2018; Nee et al., 2007). As previous recognized, this appears to be an accidental by-product of imaging techniques and accessibility to more sensitive hardware (Johansen-Berg, 2013; O’Callaghan et al., 2014; Forstmann et al., 2016). Studying the contribution of subcortical nuclei with MRI is inherently more difficult than the cortex simply due to their distance to the head coils. Lower field strengths are further disadvantaged due to the lack of penetration and therefore sensitivity here (Collins and Smith, 2001; Vaughan et al., 2001). The picture is further complicated by the need for specific contrasts in order to be able to accurately delineate some of these iron-rich nuclei such as the STN and SN (Keel et al., 2012; Keukens et al., 2017, 2018; Shroff et al., 2009). Due to the differences in iron content the subcortex also requires slightly different fMRI acquisition parameters to optimize the BOLD contrast sensitivity (e.g., de Hollander et al., 2017; Miletic et al., 2020).

The goal of this meta-analysis is to investigate the overlap and differences in cortical and subcortical contributions to recent fMRI studies of interference resolution and global inhibition. A number of fMRI meta-analysis on the topic of cognitive control have been conducted in the past (e.g., Cieslik et al., 2015; Criaud and Boulinguez, 2013; Cavazza et al., 2020; Guo et al., 2018; Huang et al., 2020; Hung et al., 2018; Niendam et al., 2012; Rae et al., 2014; Song et al., 2017; Swick et al., 2011; Xu et al., 2016; Zhang et al., 2017). However, as a number of these meta-analysis either included a low number of studies (Eickhoff et al., 2016; Muller et al., 2018), used a software version of gingerALE that was later shown to contain a number of implementation errors (Eickhoff et al., 2017; Garrison et al., 2019), or included studies from the early 90’s and early 00’s that used 1.5 Tesla (T) MRI (de Hollander et al., 2017; Krasnow et al., 2003; van der Zwaag et al., 2009). So far it is perhaps not surprising that the meta-analytical evidence for the subcortical involvement is limited.

Here, we set out to compare activation patterns in the tasks used to tap into these two subtypes of cognitive control, with a main focus on subcortical involvement. To that end we employed a fairly strict list of inclusion criteria to facilitate the inclusion of studies for which it was a priori conceivable that they reported subcortical activations with high anatomical precision. Accordingly, we only included studies from the last decade, that employed a high spatial resolution fMRI acquisition protocol on 3 T or higher field-strength MRI with little smoothing. To maximize the number of studies given these demanding criteria, we conducted a comprehensive literature search for experiments investigating interference and inhibition tasks and convolved the results using activation likelihood estimation (ALE).

2. Materials and methods

2.1. Comprehensive literature search

2.1.1. Paradigms included

We included six different paradigms in the meta-analysis that are thought to tap into interference and inhibition mechanisms, namely the Eriksen Flanker, Simon, Stroop, Multi-Source Interference, Go/No-Go and Stop-Signal tasks. The selection of tasks was based on a number of previous meta-analysis focussing on interference and inhibition (e.g., Nee et al., 2007; Swick et al., 2011; Song et al., 2017; Li et al., 2017; Hung et al., 2018).

2.1.2. Interference tasks

Eriksen Flanker task: a paradigm in which participants are shown a central target stimulus flanked by a number of adjacent distractors. The participants are instructed to press a button associated with the target stimulus. A trial is congruent if the distractors are identical to the central target stimulus, whereas the trial is incongruent if the distractors differ from the target stimulus.

Simon task: a paradigm in which participants have to respond to a given stimulus with a given button press, irrespective of the location of the stimulus. The trial is congruent if the location of the stimulus is on the same side as the correct response hand, whereas the trial is incongruent if the stimulus is on the contralateral side of the correct response hand.

Stroop task: in the classic Stroop task participants have to read a word while ignoring the font colour. The trial is congruent if the meaning of the word and the font colour are identical, whereas the trial is incongruent if they differ. Since the original paper in 1935 several variants such as the numerical and affective Stroop task have been developed. We chose not to discard any Stroop variants as we were interested in general inhibition and interference processes.

Multi-source interference task: a paradigm in which different aspects of the Stroop, Eriksen Flanker and Simon tasks are combined. Participants are shown three different items and are instructed to indicate which item differs from the other two by pressing a button. Depending on the relative font size, type of distractor or location of the target relative to the response finger a trial is either congruent or incongruent.

2.1.3. Inhibition tasks

Go/No-Go task: a paradigm in which participants have to respond to a frequent go stimulus while withholding their response to an infrequent no-go stimulus. Due to the frequent nature of the go stimuli, a prepotent response needs to be suppressed during the no-go stimulus.

Stop-Signal task: a paradigm in which participants need to respond to a given stimulus while having to inhibit their response when an infrequent stop signal is subsequently presented.

2.1.4. Inclusion criteria

All the articles found by the query search were read by two raters (SJSI and MCK) and either kept or discarded based on our predetermined inclusion criteria:

1. the study was published in a peer-reviewed English language journal between the 1st of January 2010 and the 4th of May 2020 (date of the query),
2. the study employed fMRI in healthy adults; the results obtained from patients and children (17 years and younger) were excluded. When studies with patients included a healthy control group, the data of these healthy controls were included if the results were reported separately or if the authors provided us with the necessary information upon request,
3. participants engaged in an Eriksen Flanker, go/no-go, multi-source interference, Simon, stop-signal or Stroop task where the following contrasts were reported or provided by the authors on request: Eriksen Flanker: Incongruent > Congruent Go/No-Go: no-go > go Multi-Source interference task: Incongruent > Congruent Simon: Incompatible > neutral; Incompatible > Compatible Stop-signal task: successful stop > go Stroop: Incongruent > neutral; Incongruent > Congruent

For all contrasts, if there was an affective manipulation, we only included the neutral or control trials.

4. the event related fMRI data was acquired at 3 T or above,
5. the fMRI images were acquired whole brain at a resolution of 3 mm or lower, where the voxel geometry was isotropic or near-isotropic (e.g. less than 10 % deviation along the three edges of the voxel). This means that a voxel size of $2.5 \times 2.5 \times 3.0$ is excluded but $2.5 \times $
2.5 × 2.75 is included (Mulder et al., 2019). The voxel size was determined without taking the interslice gap into account.

A GLM voxel-based approach was used to statistically analyse the fMRI data while using a maximum Gaussian smoothing kernel of 8 mm FWHM. This maximum smoothing kernel is between 2–3 times the maximum size of the voxel and is thought to be a reasonable trade-off between robust statistical group level results and the reduction of anatomical specificity (Mikl et al., 2008; Pajula and Tohka, 2014).

The whole-brain activations are reported as 3D coordinates in stereotactic space of Talairach or the Montreal Neurological Institute (MNI).

Single-subject reports and experiments where the between-group effects relate to handedness, sex and genotype were excluded. All relevant reviews and meta-analysis that were included in the above search were identified based on their abstract and cross-referenced to identify other potential empirical papers.

2.1.5. Search strategy

An exhaustive literature search was conducted using the PyMed and Neurosynth python modules within Python. PyMed is a search tool used for querying the PubMed database. The Neurosynth module queries the Neurosynth fMRI database. The query date for both searches was 4th May 2020.

The following keyword terms were used to query the PubMed database using the Entrez query tool from the Bio module in Python: ‘interference’, ‘interference control’, ‘conflict’, ‘conflict control’, ‘cognitive control’, ‘stroop’, ‘Simon’, ‘flanker’, ‘stop-signal’, ‘stop signal’, ‘stop task’, ‘stop-signal reaction time’, ‘stop signal reaction time’, ‘go/no go’, ‘go no go’, ‘go/no-go’, ‘go/no-go’, ‘go-no-go’, ‘selective inhibition’, ‘global inhibition’, ‘inhibition’, ‘response inhibition’, ‘inhibitory control’, ‘multi source interference task’, ‘msit’ and ‘multi-source interference task’. These keywords were coupled with further search terms to limit our results to only fMRI studies: “fmri”, “functional mri” and “functional magnetic resonance imaging”. Due to the co-occurrence search strategy that PubMed uses; we used all combinations of these two search term lists (81 in total) to ensure that we found as many potential articles as possible. For Neurosynth, we queried the database using both their innate feature list and also searching their database using the Entrez query tool from the Bio module in Python:

2.2. Activation likelihood estimation

2.2.1. Contrasts

Given the number of studies that we identified, we were able to compute the following main interference and inhibition contrasts (Eickhoff et al., 2010): Incongruent > Congruent (based on 25 studies with 29 experiments, 387 foci and 834 unique subjects) and Stop|NoGo > Go (32 studies with 44 experiments, 945 foci and 865 unique subjects). While there were too few studies per task to warrant a robust comparison between the different tasks, an exploratory comparison was done between the Go/No-Go and Stop-Signal tasks. There were four studies which reported the coordinates in Talairach space and were converted to MNI using the Lancaster transform as implemented in GingerALE (V.3.0.2; Lancaster et al., 2007).

2.2.2. NiMARE parameters

An activation likelihood estimation (ALE; Eickhoff et al., 2012; Fonov et al., 2011, 2009; Turkeltaub et al., 2002, 2012) meta-analysis was performed using NiMARE (V.0.0.5; Salo et al., 2020). Modeled activation maps were generated for each experiment by convolving each focus with a Gaussian kernel determined by sample size. For voxels with overlapping kernels, the maximum value was retained. The modeled activation maps were rendered in MNI 152 space (Fonov et al., 2011, 2009) at 2 × 2 × 2 mm resolution. A map of ALE values was then computed for the sample as the union of modeled activation values across experiments. Voxel-wise statistical significance was determined based on an analytically derived null distribution using the method described in Eickhoff et al. (2012), prior to multiple comparisons correction. A cluster-forming threshold of p < 0.001 was used to perform cluster-level FWE correction. 10,000 iterations were performed to estimate a null distribution of cluster sizes, in which the locations of coordinates were randomly drawn from a grey matter template and the maximum cluster size was recorded after applying an uncorrected cluster-forming threshold of p < 0.001. The negative log-transformed p-value for each cluster in the thresholded map was determined based on the cluster sizes. See Fig. 2 for a schematic of the ALE method employed for the main contrasts.

Following dataset-specific ALE meta-analyses, a subtraction analysis with 10,000 iterations was performed to compare the two datasets according to the procedure from Laird et al. (2005). In short, the subtraction analysis entailed that all experiments that contributed to the initial contrast were pooled and randomized over two groups. The ALE values for these two randomly assigned groups were then calculated, and the difference between these ALE values was recorded per voxel. This process was repeated 10,000 times and resulted in a null distribution for the difference in ALE values. The actual observed difference between the two contrasts was then compared to the null-distribution and resulted in a Z-value map. As there is no established method for multiple comparison corrections for ALE difference maps a conservative threshold of p < 0.001 was used to extract the clusters (Eickhoff et al., 2011). Note that contrary to GingerALE the subtraction analysis in
NiMARE considers all voxels instead of only evaluating the voxels that were significant in the main contrasts. As such the subtraction analysis looks at the whole brain difference between the two contrasts and can result in clusters that were not found in the main ALE contrasts. The table of clusters was extracted using AtlasReader (V.0.1.2; Notter et al., 2019) using the resulting Z-map, a respective threshold of 1.645 or 3.091 for the main and subtraction analysis which corresponds to the one-sided Z-value, with a 95% and 99.9% confidence interval and a minimum cluster size of 64mm³. Since cluster-level inference was used for the main contrasts, the cluster itself has an associated probability and subpeaks are not meaningful (Woo et al., 2014). As such, all voxels that are part of a given cluster are set to the cluster-level Z-value significance and therefore the entire cluster is set to a single cluster-level significant value. The reported cluster coordinates therefore correspond to the centre of mass (COM) and not to the peak Z-value of a given cluster.

2.2.3. Anatomical labels

As the clusters can span across a number of distinct cortical and subcortical areas, we chose to report the anatomical labels for which the cluster overlaps instead of simplifying a cluster to a single COM.
### Table 1
A summary of the included studies per domain.

| Domain | Task | Authors | Year | Number of participants | Gender ratio (f/m) | Mean Age (SD) | Field strength (T) | Smoothing FWHM (mm) | Voxel resolution (mm) | Ratio of Salient events |
|--------|------|---------|------|------------------------|-------------------|---------------|-------------------|-------------------|------------------|-----------------------|
| Interference | Flanker | Panagiotaropoulou et al. (2019) | 2019 | 30 | 7 | 27.8 (7.7) | 3 | 8 | 3 × 3 × 3 | 50/50 |
| Flanker | Siemann et al. (2016) | 2016 | 19 | ns | | 33.3 (8.2) | 3 | 8 | 3 × 3 × 3 | 50/50 |
| Flanker | Voergler et al. (2016) | 2016 | 27 | 9 | | 66.2 (7.3) | 3 | 4 | 3 × 3 × 3 | 50/50 |
| Flanker | Won et al. (2019) | 2019 | 32 | 24 | | 36.5 (7.1) | 3 | 8 | 3 × 3 × 3 | 50/50 |
| Flanker | Yamamoto et al. (2018) | 2018 | 38 | 15 | | 32 (10) | 3 | 8 | 3 × 3 × 3 | 50/50 |
| Stroop | Taylor et al. (2016) | 2015 | 18 | 10 | | 21.3 (ms) | 3 | 8 | 3 × 3 × 3 | 50/50 |
| Stroop | Robertson et al. (2015) | 2015 | 16 | 8 | | 23 (ms) | 3 | 8 | 3 × 3 × 3 | 50/50 |
| Stroop | Taylor et al. (2016) | 2016 | 16 | 6 | | 24.2 (4.7) | 7 | 6 | 2.5 × 2.5 × 2.5 | 50/50 |
| Stroop | Wagner et al. (2013) | 2013 | 34 | 28 | | 24.1 (6.4) | 3 | 8 | 2.7 × 2.7 × 2.7 | 50/50 |
| Inhibition | Go/NoGo | Asci et al. (2019) | 2019 | 24 | 16 | 23.4 (2.8) | 3 | 7 | 3 × 3 × 3 | 50/50 |
| Go/NoGo | Brown et al. (2015) | 2012 | 20 | 13 | | 22.5 (4.7) | 4.7 | 8 | 3 × 3 × 3 | 20/80 |
| Go/NoGo | Chiu and Egner (2015) | 2015 | 24 | 10 | | 24.4 (4.3) | 3 | 8 | 3 × 3 × 3 | 50/50 |
| Go/NoGo | Gonzalez Alam et al. (2018) | 2018 | 27 | 19 | | 20.7 (2.2) | 3 | 5 | 3 × 3 × 3 | 20/80 |
| Go/NoGo | Kohler et al. (2018) | 2018 | 33 | 17 | | 26.8 (5.2) | 3 | 4 | 1.4 × 1.4 × 1.4 | 26/74 |
| Go/NoGo | Mehren et al. (2019) | 2019 | 20 | 4 | | 29.5 (7.0) | 3 | 8 | 3 × 3 × 3 | 13/87 |
| Go/NoGo | Morein-Zamir et al. (2014) | 2014 | 21 | 6 | | 28.6 (7.0) | 3 | 6 | 3 × 3 × 3 | 13/87 |
| Go/NoGo | Rodriguez-Nieto et al. (2019) | 2019 | 22 | 0 | | 24.8 (4.8) | 3 | 6 | 3 × 3 × 3 | 25/75 |
| Go/NoGo | Rothmayr et al. (2011) | 2011 | 12 | 7 | | 23.7 (ms) | 3 | 8 | 3 × 3 × 3 | 20/80 |
| Go/NoGo | Sebastian et al. (2012) | 2012 | 24 | 13 | | 30.3 (8.1) | 3 | 8 | 3 × 3 × 3 | 29/71 |
| Go/NoGo | Sebastian et al. (2013b) | 2013b | 49 | 30 | | 24.7 (3.1) | 3 | 6 | 2.5 × 2.5 × 2.5 | 50/50 |

(continued on next page)
Table 1 (continued)

| Domain | Task | Authors | Year | Number of participants | Gender ratio (f) | Mean Age (SD) | Field strength (T) | Smoothing FWHM (mm) | Voxel resolution (mm) | Ratio of Salient events |
|--------|------|---------|------|-------------------------|------------------|-------------|---------------------|----------------------|-----------------------|------------------------|
| Go/NoGo | Go/NoGo | Sebastian et al. (2013a) | 2013a | 24 | 15 | 40.0 (17.1) | 3 | 8 | 3 × 3 × 3 | 29/71 |
| Go/NoGo | Go/NoGo | Rodriguez-Nieto et al. (2019) | 2019 | 22 | 0 | 24.8 (4.8) | 3 | 6 | 3 × 3 × 3 | 25/75 |
| Go/NoGo | Go/NoGo | Yoshida et al. (2013) | 2013 | 19 | 9 | 22.5 (4.2) | 3 | 8 | 3 × 3 × 3 | 20/80 |
| SST | Boehler et al. (2010) | 2010 | 15 | 9 | 22.9 (ms) | 3 | 8 | 3 × 3 × 3 | 20/80 |
| SST | Boehler et al. (2014) | 2014 | 16 | 15 | 22.8 (ms) | 3 | 8 | 3 × 3 × 3 | 36/64 |
| SST | Eijskjer et al. (2019) | 2019 | 21 | 17 | 32.4 | 3 | 8 | 3 × 3 × 3 | 25/75 |
| SST | Fujimoto et al. (2020) | 2020 | 20 | 10 | 26.6 (9.2) | 3 | 6 | 2 × 2 × 2 | 25/75 |
| SST | Gaiillard et al. (2020) | 2020 | 38 | 23 | 26.6 (7.2)* | 3 | 8 | 3 × 3 × 3 | 29/71 |
| SST | Hampshire et al. (2010) | 2010 | 14 | ns | n*** | 3 | 8 | 3 × 3 × 3 | 26/74 |
| SST | Jahafari et al. (2015) | 2015 | 23 | 16 | 21.6 (1.7) | 3 | 5 | 3 × 3 × 3 | 30/70 |
| SST | Kampa et al. (2020) | 2020 | 47 | 30 | 24.7 (3.1) | 3 | 6 | 2.5 × 2.5 × 2.5 | 25/75 |
| SST | Lorenz et al. (2015) | 2015 | 38 | 19 | 47.3 (19.3) | 3 | 7 | 3 × 3 × 3 | 25/75 |
| SST | Mohammadi et al. (2015) | 2015 | 17 | 7 | 53 (ms) | 3 | 5 | 3 × 3 × 3 | 25/75 |
| SST | Morein-Zamir et al. (2015) | 2015 | 32 | 14 | 30.9 (8.1) | 3 | 8 | 3 × 3 × 3 | 17/83 |
| SST | Osada et al. (2019) | 2019 | 14 | 7 | 28.1 (9.9) | 3 | 6 | 2 × 2 × 2 | 25/75 |
| SST | Rae et al. (2014) | 2014 | 17 | 5 | 28 (ms) | 3 | 8 | 3 × 3 × 3 | 25/75 |
| SST | Schel et al. (2014) | 2014 | 24 | 13 | 21.5 (2.4) | 3 | 8 | 2.75 × 2.75 × 2.75 | 25/75 |
| SST | Sebastian et al. (2012) | 2012 | 24 | 13 | 30.3 (8.1) | 3 | 8 | 3 × 3 × 3 | 25/75 |
| SST | Sebastian et al. (2016) | 2016 | 28 | 17 | 26.1 (5.7) | 3 | 8 | 3 × 3 × 3 | 25/75 |
| SST | Sebastian et al. (2013b) | 2013b | 49 | 30 | 40.0 (17.1) | 3 | 8 | 3 × 3 × 3 | 25/75 |
| SST | Sebastian et al. (2013a) | 2013a | 24 | 15 | 27.4 (5.6) | 3 | 8 | 3 × 3 × 3 | 25/75 |
| SST | Tabu et al. (2011) | 2011 | 13 | 5 | 27.5 (5.2) | 3 | 6 | 3 × 3 × 3 | 25/75 |
| SST | Tabu et al. (2012) | 2012 | 13 | 2 | 30.7 (4.1) | 3 | 6 | 3 × 3 × 3 | 25/75 |
| SST | van Eijk et al. (2015) | 2015 | 18 | 18 | 25.3 (4.5) | 3 | 6 | 3 × 3 × 3 | 25/75 |

A single study could include multiple groups of participants and each group of participants could be included in multiple experiments. The gender ratio indicates the number of female participants of the entire sample. The mean age and standard deviation (SD) of the participants, rounded to the nearest decimal. The field strength in Tesla (T) of the MRI scanner used to acquire the functional MRI data. The full width half-maximum (FWHM) smoothing kernel in mm used to pre-process the fMRI data. The voxel size in mm (x, y, z) of the acquired fMRI dataset, either as reported or as determined based on the matrix size and field of view (FOV). Coordinates and/or other missing information was acquired via personal communication. *Note that Salzer et al. (2019) did not find any significant clusters and is therefore a null result. **The mean age and standard deviation are based on the calculated pooled mean and SD of the male and female participants. ***The initial sample had a mean age above 18. A number of participants were however excluded and no demographic information regarding age was provided of the final sample. Given the mean age of the entire sample we made the assumption that the study included adults. MSIT: Multi-Source interference task; SST: Stop Signal Task; Ns: not stated. Ratio of salient events: x/y where x corresponds to the number of salient events (e.g., the incongruent, stop, or NoGo trials) and y corresponds to the number of number of control events (e.g., the congruent or go trials).

2.3. Open science

A python notebook to query PubMed and Neurosynth is provided on the following link. All syntax used to run the ALE analyses with the corresponding input and output files are also provided in the following link (DOI 10.17605/OSF.IO/Y7G84).
3. Results

3.1. Main contrast results

Because each significant cluster is generally not solely within one specific brain area, we provide the main anatomical regions that overlap within each cluster. The percentage overlap of each of these structures within the significant clusters can be found in Supplementary Table 1 for each of the three atlases used (AAL2, Harvard-Oxford and Julich).

3.1.1. Interference resolution

The NiMARE ALE analysis found 9 significant activation clusters within the main contrast (Incongruent > Congruent) for the Flanker, Simon, Stroop and multi-source interference tasks (see Figs. 3 and 4). Significant clusters within this contrast included the bilateral SMA, bilateral insula, left occipital inferior lobule, left anterior intra-parietal sulcus, left IFG, left superior frontal gyrus and left superior parietal lobule (see Table 2).

3.1.2. Global inhibition

The NiMARE ALE analysis found 14 significant activation clusters within the main contrast (Stop|NoGo > Go) for the go/no-go and stop-signal tasks (see Figs. 3 and 4). Significant clusters within this contrast included the bilateral SMA, bilateral insula, left occipital inferior lobule, left anterior intra-parietal sulcus, left IFG, left superior frontal gyrus and left superior parietal lobule (see Table 2).

3.2. Comparison between interference and inhibition types

High overlap of activation clusters is found between interference and global inhibition, it should be noted that the latter appears to recruit many more regions than the former during the main contrasts for these task types. Recruitment of the bilateral SMA, bilateral Insula, and left IFG is shown for both inhibition types.

3.3. Subtraction analysis

Here, we present results firstly for the subtraction analysis of the interference-specific activations minus the inhibition-specific activations, and then the reverse of this, to indicate where these processes differ on a neural level.

3.3.1. Interference > Inhibition

The interference minus inhibition subtraction analysis displayed 3 significant clusters. The main anatomical overlap within each cluster can be seen in Table 4. The largest clusters appear to be in the left inferior parietal lobule, bilateral precuneus, and left mid cingulate cortex (see Fig. 5).
3.3.2. Inhibition > Interference

The inhibition minus interference subtraction analysis displayed 8 significant clusters. The main anatomical overlap within each cluster can be seen in Table 4. The largest clusters here appear to be in the bilateral inferior parietal lobule, bilateral frontal poles, right premotor cortex, right striatum, and the left early visual cortex (see Fig. 5).

4. Discussion

4.1. Dissociation between interference resolution and global inhibition networks

Using the meta-analytical method of ALE, we sought to shed light on our current understanding of the functional overlap between interference resolution and global inhibition in the cortex and subcortex. The meta-analysis provides an updated view on cognitive control by including only papers published in the last decade. For the interference tasks, the associated regions were the bilateral SMA, bilateral insula, left intraparietal sulcus, left superior parietal lobule, left superior frontal gyrus, left inferior occipital lobule, and the left precentral gyrus. Brain areas activated in the inhibition tasks include the bilateral insula, right IFG, bilateral precentral gyrus, right inferior temporal lobule, left fusiform gyrus, left supramarginal gyrus, bilateral SMA, visual cortex and frontal pole. The main anatomical overlap of the interference and inhibition tasks was found in the bilateral SMA and bilateral insula. Our subtraction analysis indicates that the bilateral precuneus and midcingulate cortex were implicated as distinct brain areas involved in interference resolution but not global inhibition. The subtraction analysis also revealed a number of regions involved in global inhibition that were not recruited during interference resolution, namely the bilateral inferior parietal lobule, the right premotor cortex and bilateral frontal pole. The differences in neural recruitment between the Go/No-Go and Stop-Signal task seem to follow the results as presented by Swick et al. (2011) but as stated, the number of contributing studies was low and
should not be overinterpreted.

Generally, interference resolution appears to recruit more left-lateralized and global inhibition more right-lateralized regions. Note that this lateralization pattern for interference and inhibition tasks has been reported before (Aron et al., 2014a; Aron et al., 2014b; Vanderhasselt et al., 2009; Zhang et al., 2014), although that is not always the case (Serrien and Sovijärvi-Spapé, 2013). Taken together, the results of the meta-analysis are clear-cut in terms of supporting the need for separating these subtypes of cognitive control. Although there is evidence for some overlap between the networks that subserve these mechanisms, the results here, combined with previous work (Huang et al., 2020; Hung et al., 2018; Tobia et al., 2016), largely suggests that these cognitive processes are rooted in a number of distinct cortical brain areas.

Contrary to previous findings, our results do not show activation of the ACC in either contrast. Although the ACC is commonly implicated in cognitive control (Hung et al., 2018; Mayer et al., 2012; Nee et al., 2007; Zhang et al., 2017) discrepancies have been shown (Veroude et al.,

Fig. 4. The activation clusters for the interference and inhibition ALE analysis in standard MNI space. The blue clusters correspond to the interference contrast, whereas the red clusters correspond to the inhibition contrast. The numbers indicate the Z coordinates in MNI space. R: right.
The ACC function which suggest that the ACC plays a pivotal role in conflict monitoring and action selection (Botvinick et al., 2001; Holroyd and Coles, 2008).

This is in contention to early models for functional cognitive control (Di Pellegrino et al., 2007; Fellows and Farah, 2005; Mansouri et al., 2009). This is consistent with lesion studies that indicate categorization based on the regions is not necessary for functional cognitive control (Di Pellegrino et al., 2007; Fellows and Farah, 2005; Mansouri et al., 2009). This is in contrast to early models for functional cognitive control (Di Pellegrino et al., 2007; Fellows and Farah, 2005; Mansouri et al., 2009). This is consistent with lesion studies that indicate categorization based on the regions is not necessary for functional cognitive control (Di Pellegrino et al., 2007; Fellows and Farah, 2005; Mansouri et al., 2009). This is consistent with lesion studies that indicate categorization based on the regions is not necessary for functional cognitive control (Di Pellegrino et al., 2007; Fellows and Farah, 2005; Mansouri et al., 2009). This is consistent with lesion studies that indicate categorization based on the regions is not necessary for functional cognitive control (Di Pellegrino et al., 2007; Fellows and Farah, 2005; Mansouri et al., 2009).

4.2. Subcortical involvement in cognitive control

Imaging the subcortex is notoriously difficult using standard fMRI acquisition and analysis protocols (de Hollander et al., 2017; De Hollander et al., 2015; Keuken et al., 2018; Miletić et al., 2020; Mulder et al., 2019; Torrisi et al., 2018). To account for these challenges, we only included studies that employed 3 T or higher field strengths with...
(near) isotropic voxel sizes of $3 \times 3 \times 3$ mm or smaller. Furthermore, we only included studies that processed the fMRI data with FWHM smoothing kernels that were smaller or equal to 8 mm. Due to the whole brain acquisition inclusion criteria, a number of studies had to be excluded that focussed on a number of a-priori defined subcortical regions (e.g., de Hollander et al., 2017; Miletić et al., 2020). The stringent MRI parameter inclusion criteria did not, however, result in a large number of studies that used ultra-high field MRI as 55 out of the 57 included studies employed 3 T MRI, which might not be ideal for imaging the subcortex (de Hollander et al., 2017; Forstmann et al., 2016; Isaacs et al., 2020).

Regardless of field strength, of the 73 contrasts used in the final analysis, 27 (15 within global inhibition, 12 within interference resolution) of them reported a peak coordinate within the subcortex. The average voxel volume of all included studies analysed here was 24.6 mm, which would give approximately 3–4 voxels in the STN ($82.5 \pm 22.5$ mm), 19–20 voxels in the SN ($469.9 \pm 88.8$ mm) and 34–35 in the Globus Pallidus externa (GPe; $860.3 \pm 137.7$ mm; Alkemade et al., 2020), whereas optimized UHF fMRI sequence for the subcortex can achieve voxel volumes of $3.38$ mm with relative ease (de Hollander et al., 2017; Miletić et al., 2020).

As is clear from the results, there appears to be an absence of consistent subcortical activation patterns in both the global inhibition and interference tasks. This was surprising given the intracranial recording work and recent coordinate-based fMRI meta-analyses for response inhibition (Hung et al., 2018; Zhang et al., 2017). The only evidence found for the involvement of the subcortex was the putamen (inhibition contrast, cluster 1), but no clear evidence for the thalamus or other basal nuclei, in contrast to previous single studies (Aron, 2007; Duann et al., 2009; Wimmer et al., 2015; Wright et al., 2015; Zandbelt et al., 2012).

Fig. 5. A 3D representation of the activation clusters for the subtraction analyses. A) Shows the clusters corresponding to the interference > inhibition subtraction (blue) and the clusters corresponding to the inhibition > interference subtraction (red). B) Shows the clusters for the interference > inhibition subtraction only. C) Shows the clusters for the inhibition > interference subtraction only. The three columns show the right, superior and posterior view. R: right.
and meta-analyses (Cieslik et al., 2015; Guo et al., 2018; Hung et al., 2018). The putamen has been implicated as a vital element for motor control in the process of global inhibition (Alexander et al., 1986; Zandbelt and Vink, 2010). As such it remains unclear from this meta-analysis which aspects of cognitive control are implemented in the subcortex and how these processes are shared between interference resolution and global inhibition.

It appears that as methodology has progressed in the last decade, little improvement was made toward increasing sensitivity in subcortical areas. This has made sufficient aggregation of subcortical data by standard whole brain meta-analytical methods problematic. As whole-brain acquisition usually entails sacrificing spatial resolution, whole-brain coordinate based meta-analyses may not be optimal for aggregating functional data for small subcortical regions. It should also be noted that cluster-based thresholding inherently biases against small clusters, such as those normally found in the subcortex (Woo et al., 2014). This suggests that ROI- and image-based methods may be superior for inferring subcortical contributions to cognitive mechanisms as investigated here (Colizoli et al., 2020; De Hollander et al., 2015).

As a consequence, when conducting meta-analyses focusing on the human subcortex one may use less conservative criteria (e.g., lower resolution, lower field strengths), leading to more partial voluming and low numbers of voxels in smaller structures or use stricter criteria, which results in lower sensitivity and a lower number of studies. Such a choice can be overcome by moving away from coordinate based meta-analyses and instead using analyses directed by predefined regions of interest.

4.3. Limitations of the current study

A general limitation is the anatomical specificity of the results. In a coordinate-based meta-analysis such as in the current study we only incorporate the reported peak coordinates of what is likely a much larger cluster of activation. This limitation can be addressed by conducting an image-based meta-analysis using either the raw data or statistical maps of the included studies. This would, however, require that the data is publicly shared on a data repository such as Neurovault (https://neurovault.org; Gorgolewski et al., 2015) or OpenNeuro (https://openneuro.org; Poldrack et al., 2013) which can be accompanied by a data descriptor paper (“More Bang for Your Byte,” 2014; Shaklee, 2014).

None of the data analysed here was openly available online on such websites, though most authors do make their data available upon direct request. A specific limitation of the current meta-analysis are the specific tasks that were included. Based on a number of previous meta-analysis we chose to only include the Go/No-Go and Stop-Signal task for global inhibition. Future work should extend this selection of paradigms to also include tasks such as the anticipated response inhibition task (Slater-Hammel, 1960) and countermanding saccade task (Hanes et al., 1998). Other potential tasks of interest might be the random dot motion paradigm which has been used in the past to investigate stimulus and response conflict processing (e.g., Wendelken et al., 2009). Note that ideally the number of experiments across the different paradigms which contributed to the contrast is balanced (Miller et al., 2018). Finally, due to the selection of specific tasks, the interference contrast is mostly based on equal probable salient events whereas this is approximately 1:3 for the inhibition contrast. This difference in saliency might explain the involvement of the parietal areas (and potentially the right IFG) in the interference contrast as these have been linked to attentive processing (e.g., Boehler et al., 2011).

5. Conclusion

We set out to investigate the contribution of recent, high-resolution fMRI in the study of cognitive control through an extensive meta-analysis. This has revealed a gap in the neuroscience literature pertaining to high resolution neuroimaging of interference and inhibition tasks. In particular, subcortical findings did not result in clusters that survived statistical threshold. The results presented here show large overlaps but also some discrepancies with previous work investigating the brain regions underpinning interference resolution and global inhibition. Cortically, the involvement of the insula and SMA in both mechanisms is not surprising, though the lack of significant activation in the ACC indicates that our understanding of the inhibitory and attentional networks is not yet complete. Future studies focusing on imaging the subcortex are required to shed light on the networks involved in cognitive control at a whole-brain level.

Declaration of Competing Interest

We have no competing interest to declare regarding this work.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.neubiorev.2021.07.021.

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