

**Individual Differences in Self-Focussed
Attention: Relationship to Inhibitory
Control and Intrinsic Architecture of
Large-Scale Networks.**

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Abstract

Self-relevant material presents an encoding advantage termed the self-reference effect (SRE) in which rich pre-existing schemas allow such material to be efficiently encoded. Self-relevant material is also prioritised during information processing, acting as a powerful distractor. Furthermore, activation in the Default Mode Network (DMN), engaged during self-referential processing, has been linked to errors during tasks, suggesting self-focussed attention as a potential source of distraction. The current work explored whether individuals with a stronger SRE, thought to reflect the level of articulation of one's self-schema, would perform worse at inhibitory control tasks that demand sustained attention on the external world. Study 1 and Study 2 confirmed this hypothesis suggesting that poor performance in inhibitory control tasks is at least in part due to attention being diverted towards the self. Study 2 explored the neural underpinnings of such relationships using a cross-sectional resting-state analysis. Connectivity of regions involved in self-referential processing was explored in relation to inhibitory control efficiency scores revealing that individuals with stronger coupling to right inferior frontal gyrus performed better at a Go/No-Go task. Similarly, the Frontoparietal Control Network (FPCN) was more coupled to the ventral striatum, commonly associated with self-relevance assignment, when SREs were smaller. Study 1 also found stronger coupling between DMN and executive control regions for individuals with better memory in the non-self control condition (low SRE), whereas individuals with stronger within DMN coupling had high self-memory scores (high SRE) suggesting integration between DMN and FPCN reduces self-focus. Study 3 measured self-focussed attention using the private self-consciousness scale and revealed the FPCN to be more coupled to fusiform/hippocampus in individuals with higher private self-consciousness scores, potentially reflecting episodic information in the working memory space. Overall we present substantial evidence supporting a strong relationship between self-bias and executive control both at the behavioural and neural levels.

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Author's Declaration

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de Caso, I., González, T., Jefferies, E & Smallwood, J. (in prep). Don't Forget About Me: The Self-Reference Effect and its Relationship to Inhibitory Control

Chapter 1 - Introduction

Who is the I that knows the bodily me, who has an image of myself and a sense of identity over time, who knows that I have appropriate strivings? I know all these things, and what is more, I know that I know them. But who is it who has this perspectival grasp? . . . It is much easier to feel the self than to define the self.

—G. W. Allport, *Patterns and Growth in Personality*

In an attempt to study the nature of commonly used concepts such as memory, attention or self, psychologists and philosophers have stumbled across the hidden complexity that underlies these widely used concepts. Self-consciousness, self-awareness, objective self, episodic self, are examples of this. The main focus of the current doctoral work was to study the abstract representation of one's self, i.e., the self-schema. In particular, the current research was interested in how individuals differ in the degree to which they have developed and articulated their self-schema, as well as to how this relates to the intrinsic architecture of the brain and to their inhibitory control abilities.

Evident prerequisites for the development of the self-schema are the ability to perceive the self as an object which in turn allows attention to be directed inwards. As will be discussed in future sections this objective representation of self is believed to be achieved through the semantic memory system. A safe assumption to make is that individuals who engage more in self-focused attention will more commonly recruit the self-schema, which through its interaction with episodic memory, shall result in a deeper articulation of itself by allowing its revision, reinforcement and updating. Building on previous literature exploring the enhancing role that pre-existing information in the form of schemas has on encoding and retrieval (van Kesteren, Fernández, Norris & Herman, 2010; van Kesteren et al., 2013; van Kesteren, Rijpkema, Ruiters, Morris & Fernández, 2014; Ghosh & Gilboa, 2014; Ghosh,

Moscovitch, Colella & Gilboa, 2014), we developed our research question from the assumption that a deeper articulation and engagement of the self-schema shall result in a stronger memorial advantage for material processed in relation to the self. Study 1 and Study 2 studied the relationship of this measure to inhibitory control performance. In addition, the first study explored how the magnitude of the self-reference effect relates to the functional connectivity of memory-related regions, with a particular focus on regions involved in self-referential processing. The second study instead explored the functional connectivity of inhibitory control regions in relation to the magnitude of the self-reference effect.

The first section of the introduction briefly presents some theories regarding how the objectification of self emerges (Duval & Wicklund, 1972; Mead, 1934). Due to its object-like nature this representation of self is highly related to the semantic system. Evidence that a highly resilient aspect of self, that of who we believe we are, is held as an abstraction and hence shares properties of semantic information is further presented (Klein & Lax, 2010). We then delve into reviewing the potential mechanisms underlying the emergence of the memorial advantage observed for material processed in relation to the self and introduce the neural correlates underpinning this effect. This section will help the reader understand the rationale behind using a self-descriptive task, thought to recruit the semantic self, as a means to obtain incidental memory scores reflective of the extent to which an individual has articulated their self-schema. Building on previous research demonstrating the role of the medial prefrontal cortex (mPFC) to self-referential processing and more specifically to the memorial advantage achieved through self-reference (Kelley et al., 2002; Macrae, Moran, Heatherton, Banfield & Kelley, 2004) the first empirical chapter was directed at studying whether individual differences in the magnitude of the self-reference could predict individual differences in the intrinsic architecture of this region.

After having established the legitimacy of the magnitude of the self-reference effect as an indirect measure of the degree to which one has articulated their self-schema, the next part of the introduction focusses on the detrimental aspects of excessive self-focussed attention. In particular, an overview of the evidence

demonstrating that self-relevant material acts as a powerful distractor is presented (Geller & Shaver, 1976; Moray 1959; Sui, He & Humphreys, 2012) alongside aspects of the neural mechanism underlying the salient properties of this material (Sui, Rotshtein & Humphreys, 2013a; Sui, Liu, Mevorach & Humphreys, 2013b). This doctoral thesis was particularly interested in this detrimental aspect of self-focussed attention and in particular its aim was to explore whether a direct relationship between the magnitude of the self-reference effect and an individual's performance during inhibitory control tasks could be found. This was based on the notion that good performance on inhibitory control tasks requires sustained attention on the task, achieved through restraining oneself from processing self-relevant material. Hence we hypothesised that individuals with worse performance would present a stronger self-reference effect. This prediction was behaviourally tested and confirmed in the first empirical chapter suggesting the magnitude of the self-reference effect captures one's tendency for self-focussed attention. The second empirical chapter replicated this finding and building on this existing relationship, a cross-sectional design was used to explore its neural underpinnings. In particular, the behaviour of regions involved in self-reference was studied in relation to the inhibitory control scores and similarly, the magnitude of the self-reference effect was used to explore the functional connectivity of regions involved in inhibitory control.

1.1 Philosophical Aspects of the self

1.1.1 Subjective and Objective Self

The self, like language, is inherent to the human experience. Long theorised about in theology, psychology and philosophy, innumerable notions of self exist. Although it is beyond the scope of this doctoral thesis to present an extensive review or to formulate a theory of the self, one cannot ignore a principal distinction recurrently being made in the literature. This is the notion of the self as subject, or the "I" and the self as object or the "me" (Cooper 1992; James, 1981). The self as "I" refers to the subject who is aware of the qualia being experienced. An idea or feeling that it is "I" who is having this experience; this is the subjective self. Instead, when the knower's attention

focuses on itself the “I” becomes the object of study. A meta-representation of the self is created, which constitutes the “me” or empirical self, what today is called the self-concept (Wylie 1974). Gallagher (2000) makes a similar distinction between what he calls the “minimal self” and the “narrative self”. The minimal self is defined as “an immediate subject of experience, unextended in time” (p.15) in opposition to the narrative self which depends largely on memory and language. The minimal self is pre-reflective, non-conceptual and emerges from interactions with the environment, it is also tightly linked to the sense of agency and ownership. This is the most primitive sense of self, and it constitutes the embodied self, which is independent of the use of the first person pronoun (Gallagher, 2000). Despite differences across the different theories, a general division between objective and subjective self is recurrent throughout the literature. Although some attempts have been made in studying and describing the subjective component of the self (see Gallagher, 2000) it is the memory-dependent self, the self as object that has been the target of most psychological experiments, including this doctoral thesis.

1.1.2 Objectification of Self

Considering we are interested in the object-like qualities of self, an overview of how this objectification of self is thought to emerge is briefly presented in this section. Studies on children have commonly been used to study the development of self-reference and unravel when it is that the ability to observe the self as an object first emerges. Piaget (2002) for example asked children to select which blocks were nearest to a person sat opposite them. The children, failing to see themselves as a separate entity and understand that other perspectives beyond their own exist, selected those blocks which were closest to them instead of those closest to the other individual. This is defined by Piaget (2002) as absolutism, in which “the child, ignorant of his own ego, takes his own point of view as absolute” (p.197) . For the child there are no boundaries of the self and hence fails to understand that the self is an object, leaving him devoid of self-objectification and self-consciousness.

Most explanations of how objectification of the self develops emphasize the importance of social interactions arguing towards a social origin theory. Mead (1934)

for example, believes that the individual lacks an innate ability to observe itself as an object and that this ability only becomes available through social interaction. In particular, according to Mead (1934), it is through the development of an empathic relationship that the individual learns to visualise itself from an external point of view and develops a conscious awareness of itself as an object. Duval and Wicklund (1972) however point out that Mead's social origin theory presupposes that the child is aware that other points of view different to its own exist, a presupposition that is in contradiction with the child's absolutist point of view demonstrated by Piaget (2002). Instead, Duval and Wicklund (1972) argue that at the basis of self-consciousness is a differentiation process by which, through interaction with the environment and other individuals, the child's perceptions, thoughts and actions become challenged, eventually leading to the realisation of itself as a separate and distinct entity. In both theories social interaction plays an important role in the development of self-consciousness however for Duval and Wicklund (1972) the mechanisms that allow consciousness to focus on the self are inherent to the individual and no different than those mechanisms used to focus on any other object. The objectification does not occur through taking the perspective of another, like social origin theories propose. Instead the child must first recognise that other views exist. Once the child realises this, attention can begin to be directed towards the self. It is then that objective self-awareness emerges. For Duval and Wicklund (1972) the main distinction that needs to be made refers to whether attention is focussed on the self (objective self-awareness) or whether it is focussed elsewhere (subjective self-awareness).

A main interest of the current doctoral thesis was to explore individual differences in this tendency to engage in objective self-awareness and whether, due to the internal focus of this type of cognition, we could find an impairment in tasks that require sustained external attention in those individuals with a stronger memorial advantage for items processed in relation to the self. As all instances of internal mentation, obtaining an objective measure is a challenging endeavour. The next section delves into different memory systems involved in representing the self and explains why a measure of one's memorial advantage for self-related material can act as an objective measure of self-focussed attention, an assumption that we aimed to test and confirmed in the current doctoral work by demonstrating a negative

relationship between performance at executive tasks and an individual's memorial advantage for self-related items.

1.2 The Role of Memory and the Self

An obvious prerequisite for self-consciousness is memory, for example one needs to have a memory of one's actions to reflect upon them, or of one's life events to understand where certain emotions might be rooted. Moreover, one needs a sense of how the self would judge such actions or respond to the environment, a point of reference of ideal self-behaviour. This requires the activation of different processes such as retrieval of past episodes as well as judgement of them based on a personal sense of identity. The next section will present what the main systems that give rise to the self are, i.e., which systems provide the self with knowledge about itself. As we will discuss in the future section there is a difference between the system that provides the self with memories of past behaviours (episodic) and the system that provides the self with information about who one is (semantic).

1.2.1 The Semantic Self

Within declarative memory Tulving (1972, 1985) distinguished two systems-semantic and episodic. Whereas episodic memory is set on a time and space and has a narrative, semantic memory is composed of abstractions and is context-free. As such, retrieval of semantic information lacks a source, it lacks the self-referential quality present during episodic retrieval. However, a type of semantic memory that can be consider self-referential also exists. For example, one can have a sense of one's personality, necessary to rapidly guide behaviour, or one can remember facts such as the place of birth of the self (Klein & Nichols 2012). These are both examples of self-referential information held in the semantic memory system. Whereas philosophers like Locke (1841) theorised that it was episodic memory that provided the self with a sense of continuity and consistency we now know that the semantic system also plays a fundamental role in sustaining a sense of identity. Furthermore, as we will consider shortly, it has become apparent that the semantic self displays a certain degree of independence from the episodic memory system. It is important to make this

distinction between episodic and semantic self as the task in the current doctoral work was particularly aimed at recruiting semantic aspects of the self. In particular, through the use of a self-descriptive task in which participants had to judge whether certain trait-adjectives described them or not, we aimed to measure the degree to which an individual has developed their semantic self.

Evidence supporting that the retrieval of our personal identity is independent from episodic memory comes from both neuropsychology and behavioural experiments. For example, patients with severe episodic amnesia (for example patient H.M who underwent removal of a large portion of the medial temporal lobes) maintain an accurate sense of who they are despite severe episodic impairment (Klein & Nichols, 2012). Building on this, laboratory experiments have confirmed that memory of who we are is stored independently of episodic memory (Klein, Loftus, Trafton & Fuhrman, 1992). To test this, participants were asked to rate how much certain trait adjectives described them. This descriptive task was either preceded by an autobiographical task in which subjects had to recall an episode in which they displayed such a trait, or by a semantic task. This experimental setting allowed comparison of two competing theories regarding how these trait-descriptive judgements are made in relation to episodic memory. The first theory, the pure exemplar model, hypothesised that in order to make such judgements one needs to retrieve an episode in which an exemplifying behaviour of that trait was present. This would negate the existence of a semantic self or at least its independence from the episodic system. In contrast, pure abstraction models hypothesised that there is no need to recollect an episode and that instead personality trait judgements are made by accessing information that is stored as an abstraction, as a summary. If the abstraction model is true episodic recollection of a trait-exemplifying behaviour preceding the trait-judgment condition should not necessarily facilitate the trait-judgement, a result which would suggest that access to the semantic self is somehow independent of episodic memory. By measuring and comparing response times to judgements of trait adjectives made either after an autobiographical task (exemplifying such trait) or a semantic task (control) the authors found that for highly self-descriptive traits, priming the descriptive task with the autobiographical task did

not facilitate the response of the descriptive task. Instead, in cases in which the trait was not considered part of an individual's image of self, the descriptive trials that were preceded by an autobiographical task were answered faster than if preceded by a semantic task. These results led the authors to suggest that the self holds an image of itself as an abstraction or schema composed of the highly self-descriptive traits. This image of self is independent of the episodic system and only when the trait adjective is not part of the self-schema is episodic memory necessary to make the descriptive judgement.

The cases presented above suggest that retrieval of personality traits of the self is independent of episodic memory. Whether episodic memory is necessary to build that meta-representation has also been debated. Some neuropsychological cases suggest that in addition to retrieval, encoding of these trait summaries can also occur independently of episodic memory. For example, patient K.C, who after a motorcycle accident underwent personality changes and suffered severe episodic memory impairment, was still able to accurately describe his postmorbid personality despite being unable to recall any episodes in which he displayed such personality traits (Tulving, 1993; Klein, 2004). Similarly, autistic individuals, characterised by diminished episodic memory (Bowler, Gardiner & Grice, 2000; Crane & Goddard, 2008; Lind, 2010), also seem to maintain a memory of who they are despite their episodic memory impairment. For example, patient R.J, an autistic patient with episodic performance similar to that observed in brain trauma induced amnesia, was able to report a view of himself that reliably correlated with the description given by his relatives (Klein, 2004). This suggests that the formation and updating of such self-schema can occur online and not necessarily through rehearsal and reconstruction of episodes.

Importantly, it seems like semantic self-knowledge is particularly resilient and is dissociated within the semantic system from generic knowledge about the world. In support of this, Klein describes the case of patient D.B whose amnesia expanded beyond episodic memory to the semantic memory system, but who however still maintained an intact memory of his personality (Klein, 2004; Klein, Rozendal & Cosmides, 2002). These experimental and neuropsychological cases suggest that neither the retrieval nor the acquisition of trait self-knowledge relies on episodic

memory retrieval and that instead there is a specialised system within the semantic system involved in the representation of the self. This representation of self is responsible for holding our sense of identity, as observed from the neuropsychological cases presented above, and hence should be activated whenever a judgement of either a past or present event is made, using our semantic self as a point of reference. Due to the evident role that the semantic representation of self plays in constructing a sense of who we are, part of the current doctoral thesis was targeted at measuring aspects of this representation of self. In order to engage this aspect of the self, participants were asked to decide whether certain trait-adjectives described them or not, a process that requires one to access information about one's identity. Subsequently, participants were tested on their memory for the trait-adjectives they had judged in relation to themselves. These memory scores were controlled for overall memory by subtracting memory scores for items in a control, non-self-referential condition. Note that the memory measures obtained through the self-reference paradigm were episodic memory measures (i.e., Did you see this word *before* and if so *in which condition* did you see it?) however, the difference in performance in such measures will be driven by how well the items were encoded, which as we will discuss, is reliant on the articulation of the semantic self.

We have so far presented neuropsychological and experimental evidence suggesting that an aspect of an individual's sense of identity relies heavily on a semantic representation of the self. This meta-representation of self is highly resilient and to some extent independent from the episodic memory system and will be recruited during self-descriptive trait judgments.

The following section presents evidence suggesting why memory scores for items processed when making the self-descriptive judgements can be indicative of the degree to which an individual has articulated their self-schema. It begins by presenting theories aimed at explaining mechanisms involved in successful encoding and retrieval of information. We then present studies which extrapolate these theories in order to explain why material processed in a self-referential manner presents a mnemonic advantage over other types of material. Lastly, we explain why, taking into consideration these theories, it is possible that individual differences in the memorial

advantage for self-related material might be reflecting an individual's tendency for self-focussed attention.

1.2.2 The Self-Reference Effect

Whether in an episodic or in a semantic fashion, a common finding is that relating information to the self facilitates encoding and subsequent retrieval of such information. Rogers, Kuiper and Kirker (1977) were the first to report this. By comparing memory of self-referenced items judged during a descriptive task (Does this word describe you?) with memory of items judged during a semantic task (Finding a synonym to the word) the researchers found a mnemonic advantage for self-related material. This self-reference effect has also been replicated using objects. For example, Cunningham, Turk, Macdonald and Macrae (2008) demonstrated that objects which had been assigned to the self were remembered better than objects assigned to another subject. Many other studies have repeatedly replicated this effect (e.g., Bower & Gilligan, 1979; Keenan & Baillet, 1980) giving rise to a debate about whether self-referential processing has any special properties that distinguishes it from other types of processing.

Several theories aimed at explaining the self-reference effect have been described, however, which theory best explains the phenomenon depends on the nature of the task being used to obtain the memory measures. The theory that has received most attention is the elaborative/organizational dual-process explanation (see meta-analysis by Symons & Johnson, 1997). This theory proposes that self-reference promotes both elaboration and organization, processes which cause incidental encoding and aid retrieval. Elaborating on a word results in the activation of a network of associations related to such item, it is item specific. This network then acts as a trace that can guide and facilitate retrieval of the item. According to the depth of processing literature, the richer the elaborated trace, the stronger the facilitation during retrieval (Craik & Tulving, 1975). Whereas elaborative processing promotes the encoding of item-specific information, organizational processing highlights information common to a list of items, promoting encoding of the relational information between items within a hierarchical structure. Einstein and Hunt (1980)

demonstrated that relational and item specific processing are additive processes and contribute differently to retrieval processes. To demonstrate this, they measured retrieval after using an elaborative task (judging pleasantness of words in a list), an organizational task (organise words by categories) or both and found that a combination of both tasks promoted the higher recall rates. Along with organizational theorists (e.g., Tulving, 1964), they argued that organizational processing aids retrieval by allowing the formation of schemas and that once the retrieved schema has been activated, item-processing further aids retrieval through promoting discriminatory processes.

In a second experiment Einstein and Hunt (1980) demonstrated that in addition to the type of the processing performed, the way the stimuli were presented also had an effect on retrieval. Presenting stimuli as a list of related items triggers an automatic processing of the relational properties of the items, so organization happens regardless of the presence of an organizational task or not. The effect of an organizational task would therefore be redundant and not provide any additional processing than that obtained by just reading the items in the list. If instead the material is presented as a list of individual items, elaboration processes are automatically triggered regardless of the task, and a task that promotes elaboration would not provide any additional processing. In support of this theory, when lists of related words were studied, encoding was more enhanced by an elaborative task than by an organizational task. When instead the list was composed of seemingly unrelated items then the organisational task enhanced encoding to a higher degree than the elaborative task, suggesting that both processes contribute differently to encoding and that both the task as well as the way the material was presented had an impact on memory.

Building on the findings of Einstein and Hunt (1980), Klein and Loftus (1988) included a self-referential condition and tested whether the self-referential condition acted either like an elaborative or an organisational task. The authors found that in the conditions in which the words in the list were unrelated (i.e, automatic elaboration), self-reference resulted in higher recall than elaborative processing but not in higher recall than when material was processed using a categorical task. In contrast, when the items in the list were related, self-reference enhanced recall to the

same extent than the elaborative task. Klein and Loftus (1988) concluded that self-reference is unique in the sense that it promotes both elaboration and organization, independently of how the material is processed during encoding. If deeper elaboration and organisation lead to better encoding and retrieval, as is discussed above, then individuals who have a more elaborated construct of self should show a stronger memorial advantage than those who have a less elaborated construct and hence present a stronger self-reference effect.

Deeper elaboration during encoding cannot however fully account for the self-reference effect obtained when using descriptive tasks that rely on the semantic self. For example, self-descriptive judgements have short response times (Kuiper & Rogers, 1979). If the mnemonic advantage for items judged in reference to the self over a semantic judgment was due to a deeper elaboration during encoding, one would expect longer response times during self-reference. Instead, trait-judgements, especially highly descriptive ones, produce fast responses (Judd & Kulik, 1980) suggesting that other mechanisms aside from elaboration and organization contribute to the self-reference effect.

An alternative, non-mutually exclusive explanation for the self-reference effect, is presented by Rogers, Rogers and Kuiper (1979) who suggests that the memorial advantage for self-related material is due to the fact that the self is stored in semantic memory as a prototype. According to Cantor and Mischel (1977) a prototype is “a collection of the most typical or highly related features associated with a category label..... and is thought to function as a standard around which a body of input is compared and in relation to which new input is assimilated into the set of items remembered about a given experience” (p.39). Previous research on cognitive prototypes predicts that response times for an item should be related to the degree to which the item resembles the prototype, with judgments for the more prototypical items resulting in faster responses. It also predicts that false recognitions will be more common for items that resemble the prototype (e.g., Bransford & Franks, 1971; Posner & Keele 1970).

Using descriptive self-referential tasks both of these predictions, i.e., faster response times and higher false alarm rates for prototypical items, have been met, supporting the idea that the self is stored as a prototype. For example, the more an

item was felt as being part of the prototype, the shorter the response times were (Kuiper, 1981). In addition, during retrieval, a bias was found for items which were conceptually related to the prototypical self. In particular, items which had never been presented during encoding but held a strong resemblance to the prototype were more likely to be falsely remembered (Cantor & Mischel, 1977; Nasby, 1997; Rogers et al., 1979). These findings suggest that there is a prototypical representation of self. During self-referential processing this cognitive structure is activated and, according to the prototype theory, enhances encoding by rapidly making information between the trait and the prototype salient.

The idea of a prototype is closely related to the concept of a schema in the sense that a prototype is a hypothetical item that presents the most characteristic qualities of the schema. Whereas the term schema has been loosely used across the literature a common notion is that it is a network of associations built from several episodes (Ghosh et al., 2014). So, for example, the schema of bird would contain concepts such as flying, feathers, eggs or wings. Considering this schematic bird-concept, a robin would be a more prototypical bird than an ostrich or a penguin because ostriches and penguins can't fly whereas robins can. Extensive literature has demonstrated that during information processing having prior knowledge in the form of a schema facilitates encoding as well as retrieval (Ghosh & Gilboa, 2014; Ghosh et al., 2014; van Kesteren et al, 2010; 2013; 2014). Building on this, Olson (1980) suggested that "as the semantic content of schema becomes more complex, abstract, interrelated, etc., deeper semantic encoding operations will tend to be more likely, easier and more efficient" (p.158). Taking the information so far presented, it is therefore possible that the magnitude of the self-reference effect, i.e, how much one's memory for self is better than memory for another control condition, is related to the degree to which someone has elaborated their self-schema. In particular, individuals who have more thoroughly developed their self-schema should have a stronger mnemonic advantage for self-related material than those who have not developed their self-schema as much.

Further evidence suggesting that a stronger engagement in self-focussed attention results in a stronger mnemonic advantage for self-related material comes from a study by Agatstein and Buchanan (1984). Building on the idea of a private and

public aspect of self-consciousness introduced by Fenigstein, Scheier and Buss (1975), in which the private aspect relates to examining one's behaviours, and the public to how others perceive one's self, the authors designed a new version of the trait-adjective self-reference paradigm targeted at distinguishing between a private and a public self-reference condition. The private self-referent condition asked participants to judge whether certain adjectives described them (Private self-referent), which was the same approach used in the current doctoral thesis. Agatstein and Buchanan (1984) however included a new condition in which participants had to judge whether a third person thought a certain trait-adjective described the participant (e.g., "Does Alice think you are punctual?") thereby creating a public self-referent condition. In addition to the private and public self-referent conditions, self-consciousness was also measured through self-reports and participants were split into high and low private and public self-consciousness groups. The authors found that the memory differences in both conditions was dependent on which type of self-consciousness was predominant in the individual. Those in the high public/low private self-consciousness group had better memory for the items in the public but not the private self-referent condition than those in the high private/low public self-consciousness group. This study demonstrated that the degree to which one engages in a certain type of cognition affects the ease with which the system recruited encodes information.

Building up on the idea that a stronger engagement in self-focussed cognition will result in a deeper articulation of the self-schema with a subsequent memory advantage for self-related items, the first empirical chapter of the current doctoral thesis measured the magnitude of the self-reference and explored whether differences in the self-reference effect could be correlated with the intrinsic functional architecture of certain brain regions previously related to self-related processing. The next section presents an overview of which brain regions are of special interest to the current study.

1.2.3 Neural Correlates of the Self-Reference Effect

The self-reference effect refers to the mnemonic advantage that material processed in relation to the self holds. As we have discussed so far, this advantage is

thought to emerge thanks to a pre-existing and deeply elaborated network of associations related to our self-schema that gets activated during self-referential processing. Building on this we assume that individual differences in the magnitude of the memorial advantage for self-related material are indicative of differences in the degree to which one has elaborated one's self- schema. In order to engage in such elaboration, attention will need to be focussed on the self, hence it is possible that the magnitude of the self-reference effect is capturing one's tendency for self-focussed attention. The aim of the first empirical chapter was to study whether we could capture neural correlates underlying such differences in elaboration of the self-schema.

To study neural correlates related to self-focussed attention the current doctoral thesis implemented an approach based on the intrinsic architecture of the brain. Instead of looking at isolated peak activations during tasks we were interested in studying how the way in which regions communicate between each other when the mind is free from laboratory tasks is informative of the degree to which one engages in self-focussed attention. Previous literature using this resting-state functional connectivity approach has revealed that the brain is organised into distinct networks (e.g., Yeo et al., 2011), each network being composed of regions that are highly synchronised between them and poorly synchronised with regions outside of it. We first selected regions that have been commonly associated with self-referential processing during task-based analyses and explored whether their connectivity patterns to any other areas in the brain during rest were informative of the magnitude of one's self-reference effect. The following section presents an overview of the literature that led us to select the mPFC as the region of interest in the resting-state functional connectivity analyses performed in the first empirical chapter.

1.2.3.1 Self-Referential Processing in the Medial Prefrontal Cortex

Research on the relationship between self and memory was first extended to the brain by Craik and colleagues (1999). Previous research on memory suggested a hemispheric encoding/retrieval asymmetry (Tulving, Kapur, Craik, Moscovitch & Houle, 1994) based on the observation that activation in the left prefrontal cortex was

involved during encoding. Instead, retrieval processes engaged the right prefrontal cortex. Craik and colleagues (1999) argued that episodic retrieval inherently requires reference to the self, a process which is not necessary during encoding. Building on this the researchers hypothesised that self-reference might recruit regions involved in episodic retrieval. To test this the activity during several deep processing conditions was measured, including self-reference, as well as during a superficial processing control (syllable count) and a series of contrasts were performed. When comparing self-reference to the other conditions, results revealed activation in the right prefrontal cortex, an area previously associated with episodic retrieval, pointing towards the role of the self during episodic retrieval. In addition, activation in the mPFC was also found. A similar follow up study by Kelley and colleagues (2002) failed to replicate the right prefrontal activation but argued it could be due to differences in the neuroimaging method used, with the first study using PET and the second one using fMRI. Nonetheless, the study by Kelley and colleagues (2002) did replicate activation in the mPFC, reinforcing the involvement of this area during self-referential processing and pointing towards the mPFC as the fundamental neural correlate of self-referential processing. Importantly, schema related activity has been localised mainly to the mPFC and more specifically to the ventromedial prefrontal cortex (vmPFC) (Ghosh & Gilboa 2014; Ghosh et al., 2014), overlapping with regions activated during self-referential processing, potentially related to the semantic representation of the self.

A question that naturally followed was whether activation in this area was contributing to the self-reference effect directly. To test this, Macrae and colleagues (2004) measured activity during a self-descriptive task and subsequently tested participants incidental encoding of the items presented during the descriptive task. The authors found that activation in the mPFC predicted encoding, with activation in this region being higher for items that were subsequently remembered than for those forgotten. The results of this study expanded the role of the mPFC not only to self-referential processing but also demonstrated activation in this regions to be directly related to the self-reference effect.

Based on the findings so far mentioned, the mPFC seemed like an ideal candidate for studying the relationship between the semantic self, the self-reference effect and

the brain. The studies mentioned so far focused on peak activations during self-referential processing. In the current doctoral work, we wanted to extend the literature by moving from a peak activation approach to a resting-state functional connectivity one. This approach has been used in the past, revealing how the intrinsic architecture of certain regions of the brain relates to psychological measures of functions that recruit those regions (e.g., Baird, Smallwood, Gorgolewski & Margulies, 2013; Poerio et al., 2017; Sala-Llonch et al., 2012; Seeley et al., 2007). Considering activation in the mPFC is involved in the self-reference effect, could it be possible for individual differences in the magnitude of such effect to be related to differences in the intrinsic architecture of this region? The first question of the current doctoral thesis deals with this issue by measuring the memory for items presented during a descriptive self-other reference paradigm. It then uses these memory scores as regressors of interest in seed-based functional connectivity analyses of the mPFC during the resting-state as a means to study individual differences in functional connectivity related to the self-reference effect. Results obtained from such analyses will inform the literature as to which patterns of intrinsic architecture of the mPFC relate to individuals who present an increased self-bias.

1.3 The Self and Attention

The introduction so far has argued why the magnitude of the self-reference effect might be indicative of an individual's tendency to engage in self-focussed attention. Furthermore, it has introduced studies that demonstrate an important role of the mPFC during self-referential processing leading to the first question of the current doctoral thesis: Is the functional connectivity of the mPFC related to the magnitude of the self-reference effect?

After having explored how functional connectivity patterns of regions involved in self-referential processing relate to the magnitude of the memorial advantage for self, the second question of the current work turned to explore the relationship between one's self-bias as measured through the self-reference effect and one's inhibitory control efficiency. The rationale for this question was built from the idea that attentional resources are limited (Anderson, 2004; Kahneman, 1973;), resulting in a

recurring competition between processing of internal representations and processing of external stimuli. Good performance at inhibitory control tasks require sustained attention on the external world, hence we hypothesised that individuals with a stronger self-reference effect would be less efficient at inhibitory control, a finding that would confirm that the magnitude of the self-reference is indicative of one's tendency to focus attention on the self. The following section foreshadows the relationship between self and attention, presenting evidence revealing self-relevant material to have a privileged position during information processing. In particular, we introduce evidence demonstrating that the brain perceives self-relevant material as salient, which in turn leads to the automatic reallocation of attentional resources inwards and away from the external world.

1.3.1 The Self as Salient

In addition to its mnemonic properties, the self has also been extensively studied in relation to attention. Self-relevant material is treated as particularly salient by the brain, acting as a powerful distractor by automatically capturing attentional resources. This was first demonstrated by Moray in 1959 using a dichotic listening task. During this task, participants were simultaneously presented with one set of stimuli through one ear and with another set of stimuli through the other ear and instructed to create an attentional barrier so that only the material presented through one of the sides would reach consciousness. In other words, they had to attend to one side whilst ignoring the other side. Subsequent tests on the participants' memory for material presented on the to-be-ignored side revealed that participants successfully managed to suppress processing of that material except when presented with the subject's own name, this stimulus being particularly efficient at breaking through the attentional barrier. These results demonstrated that material that is relevant to the subject has a stronger ability to automatically attract attention than other type of material and that it is therefore harder to inhibit.

Expanding on this research Geller and Shaver (1976) demonstrated that the presence of mirrors and cameras, known to increase self-focussed attention, produced more interference during a Stroop Task. This interference, measured as

longer response times, indicates that the self automatically competes for attention with the task, leading to the subsequent impairment in performance. Furthermore, the authors also compared the response times based on the self-relevance of the words and found that self-relevant words produced higher interference than neutral words. It is therefore not only one's name or self that is salient, but more generally, it seems like salience increases with the degree of self-relevance of the material.

In addition to response-time measures, the impact of self-relevance on attention has also been studied through directly measuring brain responses to material related to the self. For example, using EEG, Gray, Ambady, Lowenthal and Deldin (2004) studied the P300 event-related potential (ERP) during processing of autobiographical stimuli such as the subject's hometown or middle name. Previous research has related this ERP to selective attention (Donchin & Coles, 1988) and found that its amplitude is proportional to the degree of attentional resources demanded by the task (Johnson, 1988) as well as to the stimulus relevance to the task (Farwell & Donchin, 1991; Squires, Donchin, Herning, McCarthy, 1977). Furthermore, its amplitude varies with the "emotional value" of the stimuli (Johnston, Miller & Burleson, 1986). Based on these findings the authors measured the P300 across three conditions: during the appearance of a red dot to which the subjects had been told to attend to, a condition expected to have a large P300 ERP, and during the presentation of both self-relevant and neutral stimuli to which participants had not been instructed to attend to. Comparing the P300 across the three conditions revealed that the ERP between the red dot condition and the self-relevant condition did not differ, both of these conditions eliciting a stronger ERP than the neutral condition, hence confirming that self-relevant material automatically recruits attentional processes.

In a series of elegant experiments Sui (2012; 2013a; 2013b) has demonstrated that this effect of self-relevant material on attention does not only apply to autobiographical stimuli for which we are highly familiar. Instead, this effect is also observed for material which has been newly associated to the self during experimental conditions. To test this, different neutral shapes such as triangles or squares were assigned during the experiment to either the self or to different referents. Once the subjects had learned the shape-referent associations participants were presented pairs of shape-referents (e.g., triangle-self) and had to judge whether the presented

pairs were correct. As expected, performance was better for trials which contained the self-related shape (Sui et al., 2012). In a follow up study (Sui et al., 2013a) brain activity using fMRI was measured while subjects performed a similar shape-referent task and found that congruent self-related pairs elicited stronger activation not only in vmPFC commonly associated with self-related processing, but also in the left posterior superior temporal sulcus (LpSTS). The LpSTS is part of the ventral attentional network involved in bottom-up attentional processes (Corbetta & Shulman, 2002; DiQuattro & Geng, 2011). In other words, the LpSTS is commonly activated when attention is automatically reoriented to salient stimuli in the environment. Importantly, the strength of coupling between the vmPFC and the LpSTS increased during judgment of pairs containing the self and was correlated to the behavioural efficiency during self-shape matching trials, suggesting this pattern of connectivity plays an important role in the automatic reorientation of attention towards self-relevant material. More specifically, effective connectivity analyses revealed that vmPFC received the visual input before LpSTS and, through its projections to the attentional network region, triggered reorientation towards the self-related stimuli by recruiting LpSTS.

Inspired by the shape-referent experimental design developed by Sui and colleagues, other studies have explored the effect that self-relevance has on perception of visual stimuli. Previous research revealed how peripheral cues that trigger covert attention over stimuli enhanced the perceived contrast in the stimuli (Carrasco, Ling & Read, 2004). Building on this, Macrae, Visokomogilski, Golubickis & Sahraie (2018) used stimuli that either had self-relevance or not as the peripheral cues and found that when the cue was self-relevant there was a heightened enhanced contrast than when it wasn't, once again demonstrating that self-relevance facilitates stimulus processing.

The evidence presented above situates the self and the material it relates to in a preferential position during information processing. As such, an enhanced performance can be observed when material related to the self has to be judged or remembered. A counter side to this naturally follows. The more salient a stimulus is the more distracting it becomes. For example, Theeuwes (2010), measuring the effect on response time of distractors of different perceptual salience, demonstrated that

the most perceptually salient distractor caused the highest interference. Using a global-local hierarchical task, Sui and colleagues (2013b) have demonstrated that self-related stimuli cause a similar interference to that of perceptual salience. In this task subjects were presented with a global, big shape perimeter (e.g., square) composed of smaller local shapes (e.g., triangles). As in previous experiments, the shapes had been assigned different referents and the participants were instructed to report either the local or the global shape. In trials in which the shape assigned to the self was presented on the opposite level to which the participant was being tested on (local/global), the response time performance was similar to that observed in a preceding experiment in which local or global salience had been visually manipulated previous to the shape-referent assignation, matching the behaviour of the most salient stimuli. Using a task based on these same principles, Mevorach, Shalev, Allen and Humphreys (2008) found that activity in the left intraparietal sulcus (IPS) was higher during the trials in which the target was less salient than the distractor. Using this IPS cluster as a region of interest in a future study, Sui and colleagues (2013b) found higher activation in this region during trials in which the self-shape was presented as a distractor. These studies demonstrate that the self, and material related to it, present the same qualities as salient material and as such should act as a powerful distractor. Furthermore, an inability to suppress self-focussed attention has been related to numerous psychopathologies such as depression, anxiety or even schizophrenia and psychopathy (for a review see Ingram, 1990). Despite the different behavioural expressions of these disorders, they seem to share this common feature which Ingram (1990) describes as self-absorption: a sustained and inflexible focus on the self.

1.3.2 External Versus Internal Attention: A Network Perspective

The last decade has experienced a paradigm shift in cognitive neuroscience by which the focus of attention has expanded from solely studying peak activations during tasks to studying connectivity between regions during not only tasks but also during the resting-state. This paradigm shift introduced the idea of brain networks, a

network being composed of regions that show higher synchrony between them than with regions outside of the network. With particular interest to the current doctoral thesis, studies of resting-state functional connectivity have revealed that regions involved in self-representation such as the mPFC form part of a larger and distributed network. This network is highly active during periods of rest, i.e., when the mind is free of task execution, the reason for which it was termed the default mode network (DMN) and originally considered a task negative network (Fox et al., 2005). This task-negative perspective of the DMN rapidly shifted in face of evidence revealing DMN activation during several tasks. As previously mentioned, self-descriptive tasks activate the mPFC, one of the main hubs of the DMN (Kelley et al., 2002; Macrae et al., 2004; Northoff et al., 2006). More generally, activation in DMN regions such as medial temporal lobes or the posterior cingulate cortex has also been found during episodic and semantic retrieval (Huijbers et al., 2012; Maddock, Garret & Buonocore, 2001) or during scene reconstruction (Irish et al., 2015; Sugiura, Shah, Zilles & Fink, 2005), or in the angular gyrus during theory of mind tasks (Schurz, Radue, Aichhorn, Richlan & Perner, 2014; Seghier, 2013). In face of these findings it becomes apparent that this network is not a task-negative network but that instead it is engaged across multiple task states, especially during instances when attention is focussed on internal representations. Instead, deactivation in nodes of the DMN is commonly observed during processing of external stimuli (Raichle et al., 2001).

As a result of this competition between the internal and external worlds, internal mentation leads to a state of perceptual decoupling by which responses to external stimuli become dampened. This was elegantly demonstrated by Barron, Riby, Greer and Smallwood (2011) who using EEG measured cortical responses to both target and distractor stimuli during an oddball task. Using the amount of task-unrelated thought reported after every trial, researchers found a reduced amplitude in the P3a and P3b ERP components, commonly associated with distractor and target stimuli respectively, in individuals who reported higher task-unrelated thought. Hence, regardless of the stimuli's task relevance, during internal mentation there is a general reduction in cortical responses related to processing of external stimuli. Activation in DMN regions has also been associated with faster responses in tasks in which performance did not depend on perceptual input. Instead, when tasks

depended on perceptual input, DMN activation was linked with worse performance (Smallwood et al., 2013) further supporting the DMN's role in processing of internal representations. Similarly, as a result of perceptual decoupling, it is not surprising that DMN activation has been associated with instances of lapses of attention (Weissman, Roberts, Visscher & Woldorff, 2006), and errors during inhibitory control tasks (Li, Yan, Bergquist, Sinha, 2007). Perceptual decoupling is also indirectly inferred from the intrinsic network dynamics of the brain which display anticorrelated activity during rest between the DMN and externally oriented networks such as the dorsal attentional network (Fox et al., 2005; Fox, Zhang, Snyder & Raichle, 2009).

A third network, the FPCN, is strategically positioned between the DMN and DAN (Vincent, Kahn, Snyder, Raichle & Buckner, 2008) and can flexibly couple to either depending on environmental task demands. For example, Spreng, Stevens, Chamberlain, Gilmore & Schacter (2010) compared activation and functional connectivity during an autobiographical and a visuospatial planning task and demonstrated that the FPCN changed its coupling to either the DMN or the DAN based on task demands, being actively engaged in both tasks. During the autobiographical planning task, the DMN was active and coupled to the FPCN whereas DAN was active and coupled to the FPCN during the visuospatial planning task. These results confirmed previous literature relating regions of the FPCN to executive control. For example, the dorsolateral prefrontal cortex, a main hub of the FPCN, is highly active during working memory tasks (Levy & Goldman-Rakic, 2000), tasks which rely on inhibitory control mechanism that give processing priority to task relevant material by blocking irrelevant material from reaching consciousness. Moreover, the FPCN forms part of the executive corticostriatal loop involved in suppression of both action and thought (Alexander & Crutcher 1990; Aron et al., 2007; Haber 2016). These results, combined with a study by Finn and colleagues (2015) which revealed the functional connectivity of the FPCN to be particularly subject-specific as well as particularly predictive of behavioural performance, suggest that the functional connectivity of the FPCN might be particularly informative of an individual's ability to suppress irrelevant self-related material when necessary and instead focus on the task.

A prediction that follows and one that we set out to test in the first two empirical chapters was that, considering the effects salience has on attention,

individuals with a more salient self should present reduced performance in tasks that require sustained attention on non-self-related material. If the magnitude of the self-reference effect is indicative of the individual's tendency to direct attention towards the self, and if this increased tendency results in higher perceptual decoupling, it is possible that individuals with a higher self-reference effect will be less efficient in tasks of inhibitory control which require sustained attention on external stimuli. In the first study we confirmed a relationship between inhibitory control and the mnemonic advantage for self-related material by correlating performance on a stop signal response time task (SSRT), classically used to measure inhibitory control, and the magnitude of the self-reference effect. Once having confirmed this behavioural relationship, the second empirical chapter explored its resting-state neural underpinnings. In particular, we hypothesised that functional connectivity of regions involved in self-referential processing might predict inhibitory control efficiency. Similarly, regions involved in inhibitory control might predict the magnitude of the memorial advantage for self-related material. Overall we expected the patterns of functional connectivity obtained using this cross-sectional design to shed light on the mechanisms that underlie appropriate control over the salient self.

1.4 From an Objective Measure of Self-Focussed Attention to a Subjective Measure: The Self-Consciousness Scale

After having studied the relationship between the magnitude of the self-reference effect and the functional connectivity of regions involved in memory such as the DMN, and executive control such as the FPCN, the third study took an alternative measure of self-focussed attention. Whereas the first and second studies demonstrated that the magnitude of the self-reference effect captures an aspect of one's tendency to focus attention on the self, allowing this measure to be used as an indirect and objective measure of self-focussed attention, the third study used a classical, direct and subjective measure, namely the self-consciousness scale.

This scale, devised by Fenigstein and colleagues (1975) was designed specifically to measure individual differences in this trait. Using this questionnaire two major components of self-consciousness were obtained: a private and a public component. The private component measures an individual's tendency to focus attention on one's feelings and behaviours (e.g., "I reflect about myself a lot"), whereas the public component measures the tendency to analyse how the self is perceived by others (e.g., "I am very concerned about the way I present myself"). Despite the self is the focus of attention in both cases the public component has a social quality that the private one lacks. A third component, social anxiety, was also defined. Despite appearing as an independent component, this component was found to be mildly and consistently correlated to public self-consciousness. The authors argued that this is because public self-consciousness is a prerequisite to social anxiety, and whereas it does not automatically imply social anxiety, it is a potential by product of it.

Extensive research has demonstrated that these components have predictive value. Not surprisingly, private self-consciousness correlates with one's memorial advantage for items processed in a self-referential manner from the first person perspective (e.g., "Does punctual describe you?") (Agatstein & Buchanan, 1984; Nasby 1985). When instead subjects were asked to judge certain trait-adjectives in relation to one's self but from an outsiders' perspective (i.e., "Does Katie believe you are punctual?") items judged in this condition were better recalled in individuals who reported higher public self-consciousness (Agatstein & Buchanan, 1984).

The third empirical chapter of the current doctoral work selected large-scale networks from the brain parcellation performed by Yeo and colleagues (2011) and studied their relationship to these measures of self-focussed attention. Considering the strong relationship between self and memory and self and attention we focussed on large-scale networks involved in memory such as the DMN and the limbic network and on networks involved in executive control, i.e., the FPCN. A summary of the measurements taken in the three studies is presented in Figure 1.1

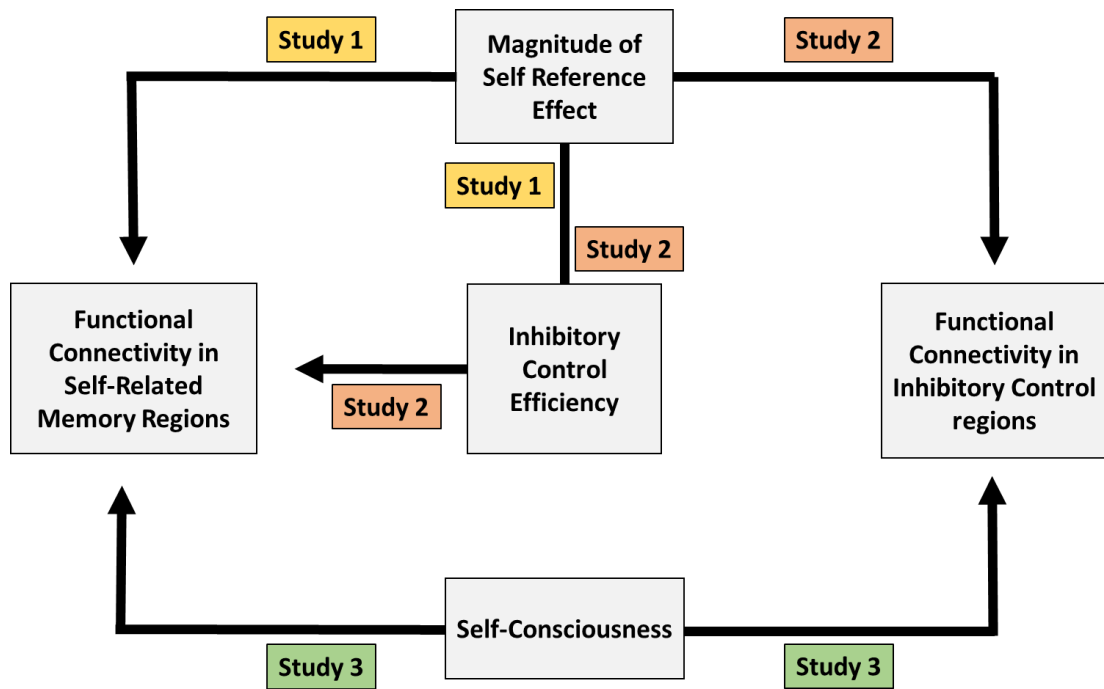


Figure 1.1: Road map of the three empirical chapters. Behaviourally, Study 1 and Study 2 explored the relationship between the magnitude of the self-reference effect and inhibitory control efficiency scores. Neurally, the magnitude of the self-reference effect was studied in relation to 1) the functional connectivity of self-related regions (Study 1) and 2) the functional connectivity of inhibitory control-related regions (Study 2). Study 2 also studied the functional connectivity of self-related regions in relation to inhibitory control efficiency scores. Study 3 measured self-consciousness scale scores and studied their relationship to the functional connectivity of self-related and inhibitory control-related regions.

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Chapter 2 - Knowing me, knowing you: Resting-State Functional Connectivity of Ventromedial Prefrontal Cortex Dissociates Memory Related to Self from a Familiar Other

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2.1 Abstract

Material related to the self, as well as to significant others, often displays mnemonic superiority through its associations with highly organized and elaborate representations. Neuroimaging studies suggest this effect is related to activation in regions of mPFC. Incidental memory scores for trait adjectives, processed in relation to the self, a good friend and David Cameron were collected. Scores for each referent were used as regressors in seed-based analyses of resting-state fMRI data performed in ventral, middle and dorsal mPFC seeds, as well as hippocampal formation. Stronger memory for self-processed items was predicted by functional connectivity between ventral mPFC, angular gyrus and middle temporal gyri. These regions are within the DMN, linked to relatively automatic aspects of memory retrieval. In contrast, memory for items processed in relation to best friends, was better in individuals whose ventral mPFC showed relatively weak connectivity with paracingulate gyrus as well as positive connectivity with lateral prefrontal and parietal regions associated with controlled retrieval. These results suggest that mechanisms responsible for memory related to ourselves and personally-familiar people are partially dissociable and reflect connections between ventral mPFC, implicated in schema-based memory, and regions implicated in more automatic and controlled aspects of retrieval.

2.2. Introduction

A fundamental aspect of the brain is its ability to encode, update and retrieve information, processes that can occur in an automatic manner or through the application of conscious effort. Both encoding and retrieval are more likely when the information is personally relevant. Strong automatic effects on memory are illustrated by the *self-reference effect* when incidental memory for material that is related to the self tends to be higher than for other types of material, such as items related to others (Kuiper & Rogers, 1979; Kelley et al., 2002) or semantically judged material (Rogers, Kuiper & Kirker, 1977). The strong automatic encoding that occurs during self-reference is thought to reflect the rich associative structure of knowledge about who we are (Symons & Johnson, 1997). Knowledge of oneself provides a powerful schema through which information can be organised during encoding and retrieval. In contrast, memory for information with a less rich associative structure is more difficult to encode and retrieve.

There is a growing body of evidence that memories with a rich associative structure depend upon the DMN, a large-scale network anchored by medial regions in the mPFC and the posterior cingulate cortex (Andrews-Hanna, 2012). The DMN, and in particular the mPFC, show high levels of activation during tasks that require self-reference (Johnson et al., 2002; Kelley et al., 2002; Macrae et al., 2004; D'Argembeau et al., 2005; Northoff et al., 2006) as well as for personally familiar referents, such as a close friend (Mitchell, Banaji, & Macrae, 2005), and when retrieving dominant semantic associations of words that come to mind relatively automatically (Binder et al., 2009; Davey et al., 2015). In all these cases memory encoding and retrieval are aided by the presence of previously formed schemas which are thought to be supported by, at least in part, the vmPFC (van Kesteren et al., 2010a; Ghosh et al., 2014). The notion that the DMN has an important role in the retrieval of information is also supported by studies that show strong coupling between the DMN and the hippocampus during successful retrieval (van Kesteren et al., 2010b; van Kesteren et al., 2012; Huijbers et al., 2011) as well as by studies that show that activity in the mPFC during the encoding phase of a self-reference paradigm predicts subsequent memory scores for items

encoded during self-reference (Macrae et al., 2004). Moreover, a related literature has shown stronger responses within the DMN during spontaneous retrieval states such as mind-wandering (Mason et al., 2007; Christoff et al., 2009; Starwarzyck et al., 2011) in which internally generated information is processed. Activity in the DMN often leads to errors during tasks that depend on a detailed processing of perceptual input (Weissman et al., 2006; Li, Bergguist & Sinh, 2007) and shows patterns of anticorrelation with regions involved in tasks involving controlled external attention at rest (Fox et al., 2005). These converging literatures are often taken as evidence that DMN can support spontaneous and undirected retrieval that interferes with ongoing processes requiring cognitive control (Anticevic et al., 2012). Together these parallel literatures implicate the DMN in the encoding and retrieval of personally relevant information into and from memory. However, recent research has also indicated that DMN sites can couple with regions implicated in executive control in situations that require memory retrieval to be controlled to suit the current demands (Spreng et al., 2014). These and other findings (e.g., Konishi et al., 2015, Krieger-Redwood, et al., 2016, Vatansever et al., 2015) suggest the DMN plays a more flexible role in memory processing than may have been recognised in the past.

To elucidate a more nuanced view of the role of the DMN in memory retrieval the current study explored whether different patterns of functional connectivity could predict incidental memory scores and in particular, whether these differ for material with different levels of personal relevance. We asked participants who had already participated in a neuroimaging session in which we recorded resting-state activity to return to the laboratory to perform an incidental memory task. They made decisions about whether trait adjectives applied to three different referents: themselves, their best friend or David Cameron (UK Prime Minister). These referents differ on their strength of personal associations which should result in higher incidental memory scores for items related to the self than their best friend and the lowest retrieval for David Cameron. In addition, since memory for similar others are known to elicit similar DMN activation and may be organised using similar or overlapping schema (Mitchell et al., 2006), accurately retrieving information about a best friend may require that competition from self-processed items may be overcome,

which have been encoded in a similar way. In contrast, items processed in relation to David Cameron will be more distinct and experience less interference. Individual variations in these scores were used to predict the functional connectivity in three sub-regions of the mPFC (ventral, middle, dorsal) taken from a decomposition of the DMN (Andrews-Hanna et al., 2010). Given evidence that the hippocampal formation is important in retrieval of information from memory, and this region is also a member of a subsystem of the DMN (Andrews-Hanna et al., 2010) this region was also selected as a seed region. In the decomposition of Andrews-Hanna et al. (2010), the hippocampal formation showed stronger connectivity to ventral mPFC than the other seed locations, and ventral mPFC has also been implicated in schema-based memory (van Kesteren et al., 2012; Spalding et al., 2015), giving rise to the prediction that this site may be particularly critical for self and best friend memory. In addition, we measured executive control via the stop signal response time task (SSRT, (Logan & Cowan, 1984; Verbruggen & Logan, 2009)) to explore whether strong automatic retrieval underpinning the self-reference effect was associated with problems in executive control.

2.3 Methods

2.3.1 Participants

Forty healthy right-handed participants were recruited through advert and either received a monetary reward of £20 or course credits. One participant had to be excluded from all analyses due to irregularities observed during fMRI scanning. Two further participants were excluded due to poor task performance, one from each task. Separate functional connectivity maps for each task were calculated with a total of 38 participants (21 males) with an average age of 22.5 (SD = 2.9) years. Approval for this project was granted by the York Neuroimaging Centre (YNiC) Ethics Committee and was in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.

2.3.2 Procedure

2.3.2.1. Self-reference paradigm.

This laboratory task involved an evaluation and a retrieval phase. During the evaluation phase (Figure 2.1A, top) participants were asked to make decisions about the association between adjectives and one of three referents ('Self', 'Best Friend' and 'David Cameron'). Adjectives were presented sequentially on-screen and participants were required to indicate whether each adjective applied to a particular referent by pressing 'Y' with the index finger of the right hand for 'yes' or 'N' with the index finger of the left hand for 'no'. For each category, participants were presented with a list of 18 unique adjectives presented in separate blocks and the order in which each category was presented was counterbalanced across participants. Each of the 18-item lists was also rotated across the different referents and the order of item presentation within each block was randomised. Stimuli were separated by an inter-stimulus interval of 2500ms during which participants were shown a blank screen with a fixation cross. Following the evaluation phase, subjects were presented with a surprise retrieval test in which they were sequentially shown words and asked whether or not that particular item had been presented in the previous phase. This retrieval phase (Figure 2.1A, bottom) contained all the words from the previous stage of the experiment, plus an equal number of new words. Items were presented in a random order and participants had to either press 'Y' if they thought the word had appeared before or 'N' if they thought it was a new word. All words were selected from a pool of normalized personality trait adjectives with meaningfulness and likeability ratings (Anderson, 1968). Positive, negative and neutral adjectives with the highest meaningfulness rating were selected for this experiment. Correct memory for each referent was calculated by subtracting the relative number of false alarms from the total number of correctly retrieved items.

2.3.2.2. Stop signal response time task (SSRT).

We developed a version of a stop-signal task (Logan & Cowan, 1984; Verbruggen & Logan, 2009) using PsychoPy (Peirce, 2007). Figure 2.1B presents a schematic representation of the trial sequence for the task. The task featured arrowheads pointing either to the left (<) or to the right (>) staying on the screen for 1000 msec independently of RT and interleaved by a 500 msec fixation cross. Participants were instructed to respond as quickly as they could, using the left and right arrow keys for the left and right arrowheads, respectively. Participants were also instructed to withhold their response when they heard a beeping sound (the stop signal) accompanying the arrowhead stimuli, which occurred in 20% of the trials (stop signal trials); the latency between the beep and the arrowhead presentation (stop signal delay or SSD) was initially set at 250 msec and was then varied with a staircase tracking procedure: when inhibition was successful and participants correctly withheld response in stop signal trials, SSD was increased by 50 msec; when inhibition was unsuccessful, SSD was decreased by 50 msec. Participants initially received on-screen instructions, followed by a brief practice session (20 trials) and then moved on to the experimental session, which was composed of 150 trials divided in two equal blocks, allowing participants a quick break in between. The whole task lasted approximately 7 minutes.

For each participant, a Stop Signal Response Time (SSRT) score was calculated by subtracting mean SSD from the untrimmed mean RT (Logan, Schachar, & Tannock, 1997). Given the wide variance of error percentage in participants a Stop Signal Efficiency score was also calculated by dividing the SSRT score by the proportion of correct stop-signal trial responses. One participant with a stop-signal trial error percentage higher than 33% was excluded from the analysis.

2.3.3 Resting-state

2.3.3.1. Scan acquisition

Functional MRI data was acquired independent of task stimulus on a 3 Tesla GE scanner. Participants observed a fixation cross for a scan that lasted 7 minutes. The scan had a repetition time of 2 seconds, resulting in 210 volumes. We used interleaved slice-timing and isotropic voxel dimensions of 3 mm³ (matrix size of 64 X 64, 192mm field of view, and 32 slices) with a 0.5mm gap between slices.

2.3.3.2. Pre-processing

All fMRI preprocessing and analysis was performed using FSL. We extracted the brain from the skull using the BET toolbox for both the flair and the structural T1 weighted images and these scans were registered to standard MNI152 (2mm) space using FLIRT (Jenkinson & Smith, 2001). Prior to conducting the functional connectivity analysis, the following pre-statistics processing was applied to the resting-state data; motion correction using MCFLIRT (Jenkinson et al., 2002); slice-timing correction using Fourier-space time-series phase-shifting; non-brain removal using BET (Smith 2002); spatial smoothing using a Gaussian kernel of FWHM 6mm; grand-mean intensity normalisation of the entire 4D dataset by a single multiplicative factor; highpass temporal filtering (Gaussian-weighted least-squares straight line fitting, with sigma = 100 s; Gaussian lowpass temporal filtering, with sigma = 2.8s.)

2.3.3.3 First level analysis

Following these steps, the time series of 4 regions of interest were extracted. The seed regions corresponded to 3mm radius spheres centred around the following MNI coordinates: vmPFC (0,26,-18), anteriomedial Prefrontal Cortex (amPFC, -6,52,-2), dorsomedial Prefrontal Cortex (dmPFC, 0,52,26) and the hippocampal formation (HF+, -22,-20,-26). These locations were selected based on previous literature (Andrews-Hanna et al., 2010) that decomposes the DMN into three subsystems, each mPFC location belonging to a different subsystem. The time series for each location

were averaged and used as an explanatory variable in a subject-level functional connectivity analysis, which also included the following nuisance regressors: the first five principal time-series components extracted from white matter (WM) and cerebrospinal fluid (CSF) masks in accordance with the CompCor method (Behzadi, Restom et al. 2007) and six motion parameters. WM and CSF masks were generated by segmenting each individual's high-resolution structural image (using FAST in FSL). The default tissue probability maps, referred to as Prior Probability Maps (PPM), were registered to each individual's high-resolution structural image (T1 space) and the overlap between these PPM and the corresponding CSF and WM maps was identified. Finally, these maps were thresholded (40% for the CSF and 66% for the WM), binarized and combined. The six motion parameters were calculated in the motion-correction step during pre-processing. Linear displacements in each of the three Cartesian directions (x, y, z) and rotations around three axes (pitch, yaw, roll) were included for each individual. No global signal regression was performed (Murphy, Birn et al. 2009).

2.3.3.4. Second-level analysis.

To understand how our psychological measures varied with the connectivity of the DMN seed regions, we used FSL to conduct a group-level regression of the connectivity matrices of each seed region. In this analysis we included the mean centred scores for the retrieval of items recalled for each item type as regressors of interest, and the mean movement during the scanning was included as a covariate of no interest. This procedure was repeated in an independent analysis using the SSRT scores instead of the self-other reference task scores. In these analyses the data were processed using FEAT version 5.98 part of FSL (FMRIB's Software Library, www.fmrib.ox.ac.uk/fsl) and the analyses were carried out using FMRIB's Local Analysis of Mixed Effects (FLAME). A grey matter mask with a probability threshold of 40% was used as a pre-thresholding mask and the cluster-forming threshold was set as z-score of 2.3. For these analyses we controlled for Type I errors by controlling for the number of voxels in the brain (Worsley 2001), as well as the

number of seed regions and the two tailed nature of our comparisons yielding an alpha value of $P < .005$ FWE. The unthresholded maps from the contrasts reported in this paper are available at Neurovault at the following link: <http://neurovault.org/collections/1373/>

2.3.4 Neurosynth meta-analyses

In order to study how the patterns of functional connectivity predictive of memory obtained in the current study were related to previous neuroimaging investigations, we performed a meta-analysis using the online Neurosynth database (Yarkoni et al., 2011). We performed a meta-analytic decoding of the unthresholded maps produced in this study by uploading them onto Neurosynth. This allows the identification of the cognitive terms that are most likely to be associated with the specific image. We display the results of these terms in the form of word clouds in the relevant figures. We also performed a specific meta-analysis of the relationship between the maps produced by our experiment, and the spatial maps that are generated by studies exploring the self. We performed a meta-analysis (903 studies) of the term “self” (<http://neurosynth.org/analyses/terms/self/>) and compared the corresponding map to the connectivity maps predictive of self memory obtained in the current study.

2.4. Results

2.4.1 Behavioural results

A one-way analysis of variance (ANOVA) indicated a significant effect of referent on incidental memory performance ($F(2, 76) = 21.58, p < .001, \eta^2 = .372$, see Figure 2.1C), as measured during the retrieval phase of the self-other reference paradigm. Post-hoc Bonferroni corrected comparisons indicated that words referred to the Self were recalled better than best friend words ($p < .01$), and these were better recalled than David Cameron ($p = .05$) items. In addition, examination of the

confidence intervals for memory for David Cameron suggested it was at chance (95% CI [.46,.54], whereas memory for best friend (95% CI [.52,.60]) and self (95% CI [.61,.68]) were both above chance. Next we examined how the process of self-reference was associated with a participant's tendency for behavioural inhibition as measured by their efficiency on the SSRT. A linear regression with incidental memory for items processed in relation to the Self, Best Friend and David Cameron as independent variables and the SSRT inefficiency as the dependent variable, revealed a model that accounted for a 22% of the variance in behavioural inhibition scores [$F(3, 36) = 3.14, p < .05, r^2 = .22$]. Higher memory for the Self was associated with less efficiency on the SSRT (*standardized beta* = .47, $t(33) = 2.7, p < .01$) (Figure 2.1D). Memory scores for best friend and David Cameron items were not a reliable predictor (*standardized beta* = .153, $t(33) = 0.9, p = .35$; *standardized beta* = -.34, $t(33) = -1.9, p = 0.58$, respectively).

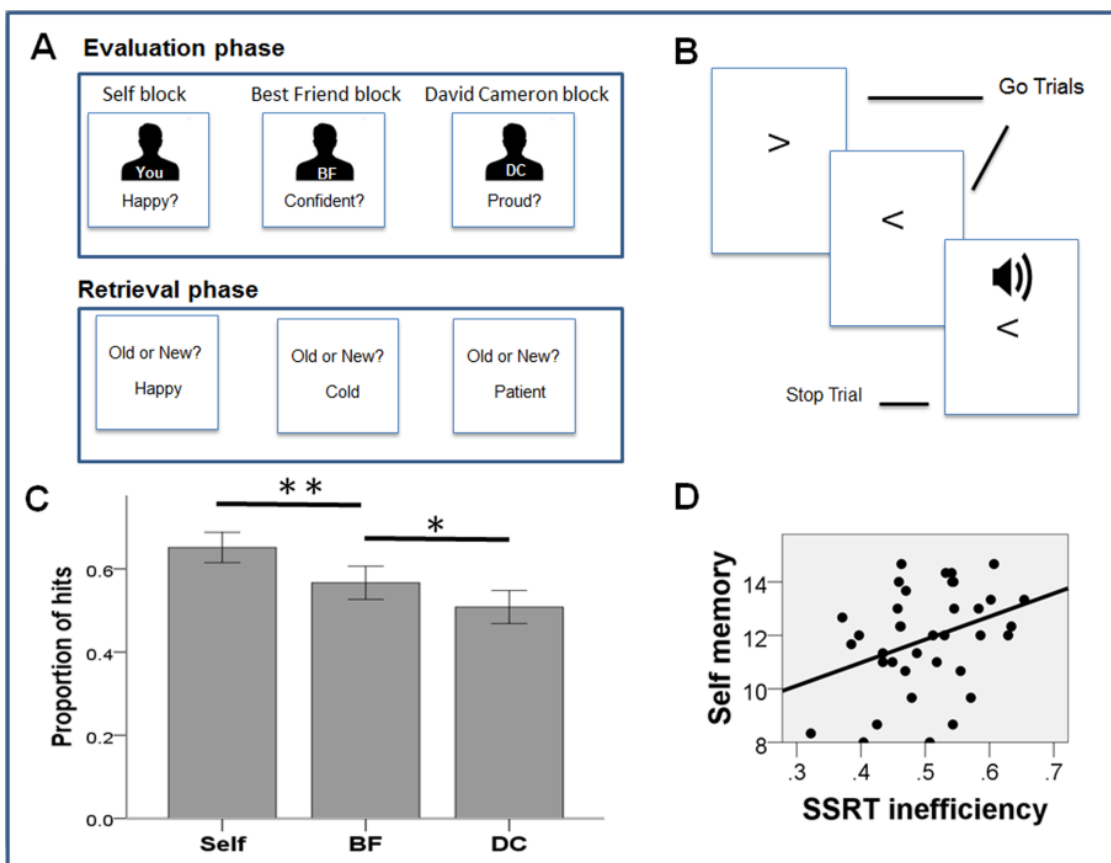


Figure 2.1: Behavioural results. A) Schematic representation of the self-reference task. Top row: Evaluation phase. Bottom row: Retrieval phase. B) Schematic representation of the stop signal response time task. C) Proportion of hits for each referent and error bars. Asterisks represent significant differences in memory performance across referents. D) Scatterplot reflecting the positive correlation between memory for self items and SSRT inefficiency. Acronyms: BF- Best friend, DC – David Cameron.

2.4.2 RS fMRI analyses

We conducted a series of multiple regressions in which the functional connectivity map of each region was the dependent variable. For each seed region we entered a measure of retrieval performance for each referent type (Self, Best Friend, David Cameron) as an explanatory variable. Independently we performed the same analysis using the SSRT efficiency scores instead of the memory scores. This SSRT measure did not reveal any patterns of functional connectivity predictive of inhibitory control for any of the seeded locations.

Figure 2.2 displays the functional connectivity group maps for each seed location and Table 1 summarises the clusters that were predictive of memory performance and that passed correction for multiple comparisons, including correction for whole-brain analysis, two-tailed tests and the number of seeded locations. Clusters that passed the first two corrections but did not pass correction for the number of seeded locations are still included in the results but are presented separately (in yellow in Figure 2.3 and Figure 2.4).

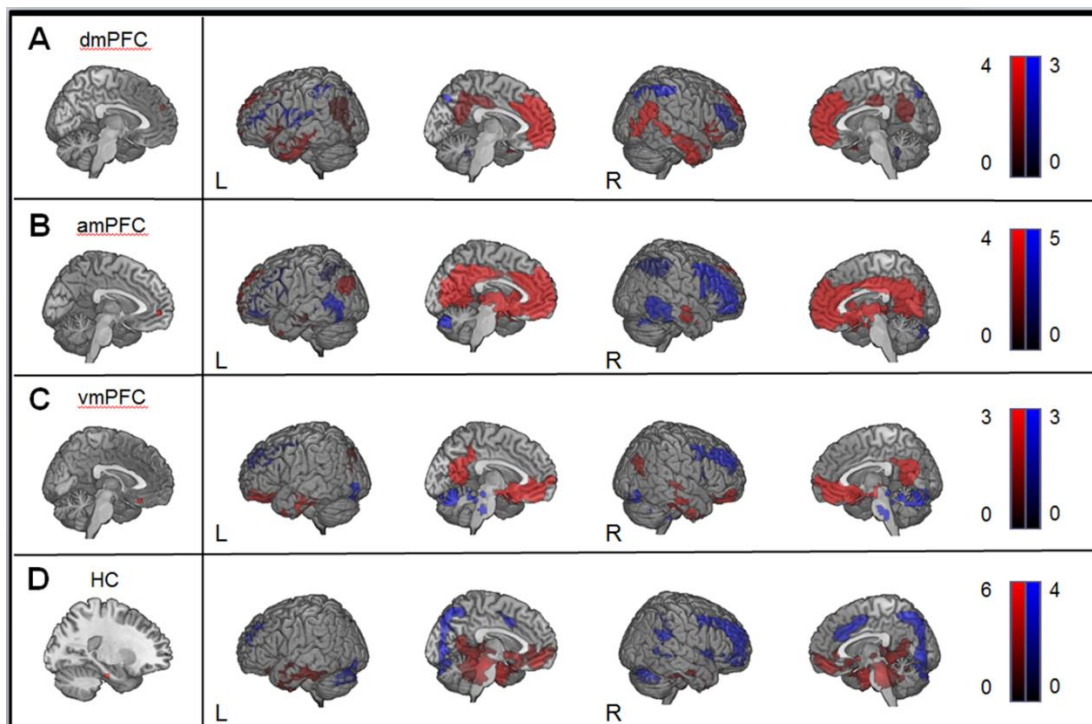


Figure 2.2: Seed regions (left column) and associated functional connectivity (FC) group maps (right column). A) Dorsomedial Prefrontal Cortex (dmPFC) 0,52,26. B) Anteromedial Prefrontal Cortex (amPFC) -6,-52,-2. C) Ventromedial Prefrontal Cortex (vmPFC) 0,26,-18. D) Hippocampal formation (HF+) -22,-20,-26.

2.4.2.1 Ventromedial Prefrontal Cortex

The functional connectivity of the vmPFC seed region predicted memory for self and best friend items. In particular, memory performance for self items was related to the functional connectivity between vmPFC and 3 clusters: right middle temporal lobe (rMTG) (Figure 2.3A, first row), left superior angular gyrus (IAG) (Figure 2.3B, first row), and left medial and anterior temporal lobe (IMTG cluster) (Figure 2.3c, first row). In all cases, stronger functional connectivity between the vmPFC and these clusters predicted better memory for self-related items as seen in the corresponding scatterplots in Figure 2.3. The rMTG cluster did not pass correction for the number of seeded locations (and is therefore shown in yellow).

In order to study the association between the clusters found and resting-state networks, these clusters were overlaid with the Yeo networks (Yeo et al., 2011). The pie charts presented in the grey panel in Figure 2.3 illustrate the overlap with the DMN (Network 7), FPCN (Network 6) and Limbic Network (Network 5) as defined by Yeo and colleagues (2011). These show the greatest overlap with the DMN (indicated in red) suggesting that functional coupling within the DMN is associated with increased memory for self-related items. In addition, the region in the rMTG shows overlaps with the FPCN (indicated in orange).

Functional connectivity between vmPFC and the paracingulate gyrus predicted relatively *poor* memory for best friend items (Figure 2.3D, first row). Overlay of this cluster with the Yeo networks revealed a strong overlap with the DMN and with the Limbic Network (indicated in purple in the corresponding pie chart in Figure 2.3). Therefore, stronger connectivity within DMN was associated with poorer memory for best friend related items, a result that stands in contrast to the findings associated with the self.

In contrast, memory for best friend items was predicted by high levels of connectivity between the vmPFC and three clusters on lateral regions of cortex. In particular, stronger functional connectivity between vmPFC and left middle frontal gyrus (IMFG) (Figure 2.4A, first row), right superior supramarginal gyrus (rSMG) (Figure

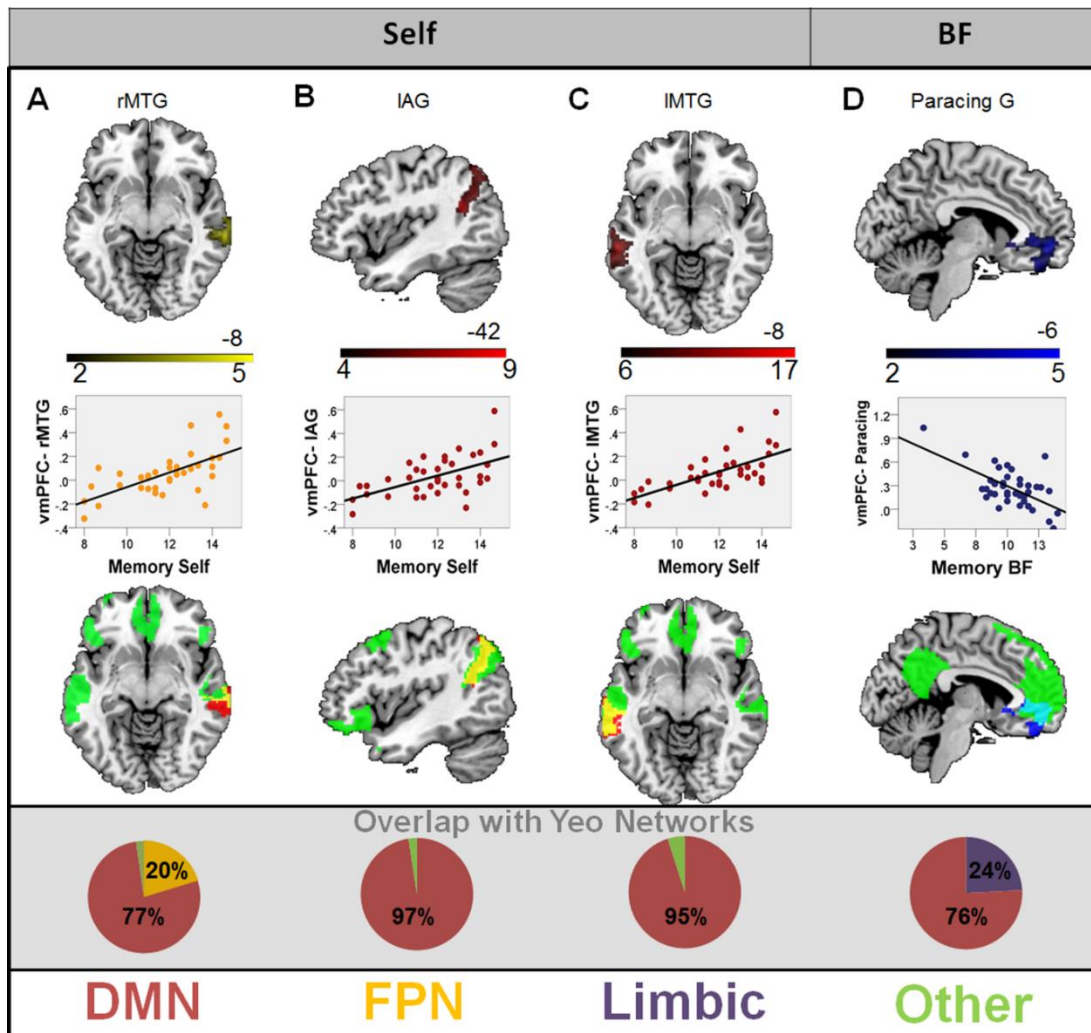


Figure 2.3: Association between ventromedial prefrontal cortex (vmPFC) functional connectivity (FC) and better self memory (Panel A, B & C) and worse Best Friend (BF) memory (Panel D). A) A region in Right Middle Temporal Gyrus (rMTG) was more coupled to vmPFC for individuals with better memory for self-related items. This cluster does not pass correction for the number of seeded locations. B) A Region of Left Angular Gyrus (IAG) showed stronger FC to vmPFC in individuals with stronger memory for self-related items. C) A Region of Left Middle Temporal Gyrus (IMTG) showed stronger FC to vmPFC for individuals with better memory for self-related items. D) A region of Paracingulate gyrus showed stronger FC to the vmPFC for individuals with reduced memory for BF items. Second Row: Scatterplots reflecting relationship between memory performance and FC between seed region and cluster. Third row: Overlap (yellow) between clusters and Default Mode Network (green). Grey panel: Pie charts and legend reflecting the percentage of the cluster that overlaps with each one the Yeo networks.

2.4B, first row) and right middle and inferior frontal gyrus (rMFG) (Figure 2.4C, first row) predicted stronger memory for best friend items. The IMFG cluster did not pass correction for the number of seeded locations. These clusters were again overlaid with the 7 Yeo resting-state networks. The overlapping proportion of each cluster and the

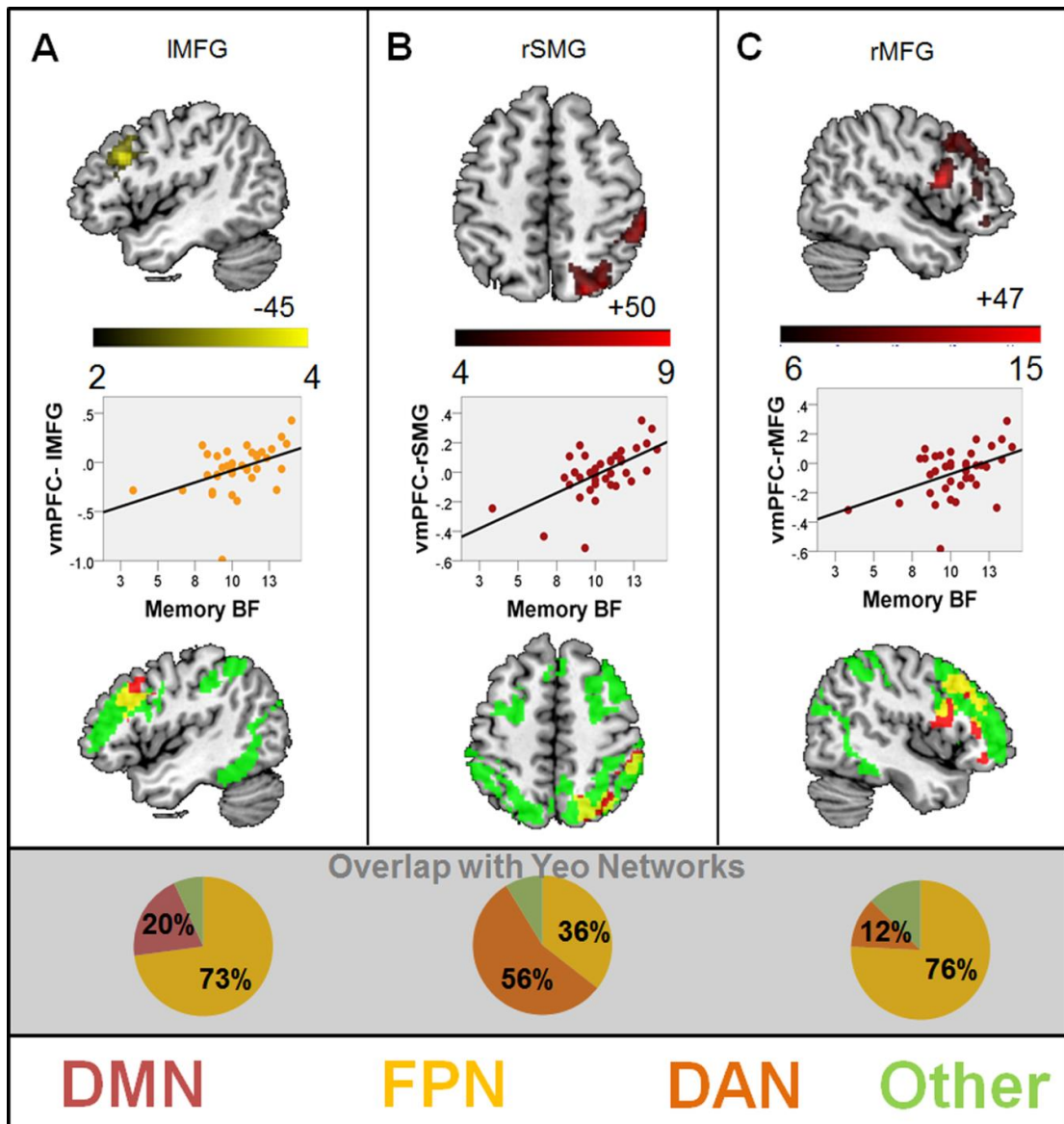


Figure 2.4: Regions showing increased functional connectivity (FC) with the ventromedial prefrontal cortex (vmPFC) showing increased memory for Best Friend (BF). A) A region of left Middle Frontal Gyrus showing stronger FC with vmPFC for individuals with better memory for BF-related items. This cluster does not pass correction for the number of seeded locations. B) A region of right Super Marginal Gyrus showing stronger FC to the vmPFC in individuals with stronger memory for BF-related items. C) Right middle frontal gyrus (rMFG) cluster with stronger FC to seed region in individuals with better memory for BF-related items (MNI: $x=47$). First row: Cluster corrected maps illustrating regions of the FC map that correlate with behaviour. Second row: Scatterplots reflecting relationship between memory performance and FC between seed region and cluster. Third row: Overlap (yellow) between clusters and the Dorsal Attention and Frontal Parietal Control Yeo networks (green). Grey panel: Pie charts and legend reflecting the percentage of the cluster that overlaps with each one the Yeo networks.

Yeo networks is displayed in the pie charts in Figure 2.4. These clusters generally overlap with regions that are important in tasks that demand externally oriented

attention such as the FPCN and the dorsal attention network (DAN). This overlap can be observed in the third row of Figure 2.4, in which the DAN and FPCN have been displayed with the same colour (green) for visualization purposes. Unlike a heightened memory for self, better retrieval of trait adjectives related to a best friend was associated with coupling in regions involved in executive control that largely fall outside the DMN.

2.4.2.2. Anteromedial Prefrontal Cortex

The functional connectivity of this brain location did not predict individual differences in memory for any of the three referents.

2.4.2.3. Dorsomedial Prefrontal Cortex

The functional connectivity of the dmPFC seed region predicted individual memory for self-related items. Stronger functional connectivity between dmPFC and a cluster located in the right occipital lobe was correlated with better memory for self-referent items (Figure 2.5A, first row). This cluster overlapped with the visual network as defined by Yeo et al.'s (2011) resting-state network analysis (see Figure 2.5).

2.4.2.4. Hippocampal Formation

The regression analyses performed on the HF+ seed revealed effects for self-related items: in particular, stronger functional connectivity between the seed region and a cluster in left ventral anterior temporal lobe (lvATL) (Figure 2.5B, first row) resulted in a better memory for self-related items. This cluster showed strong overlap with the Limbic Yeo Network (see right pie chart in Figure 2.5). Visualization of this overlap can be observed in the third row of Figure 2.5B.

2.4.3. Neurosynth Decoding Meta-Analysis

To provide a quantitative inference of our experimental data, the connectivity maps obtained for each seed region and for each regressor was decoded using NeuroSynth's dataset (<http://www.neurosynth.org/decode/>). Figure 2.6 displays all the functional terms from which the corresponding neuroimaging data from the database had correlation values bigger than 0.1 for each contrast in our data. From this meta-analytic decoding it can be seen that the functional connectivity map

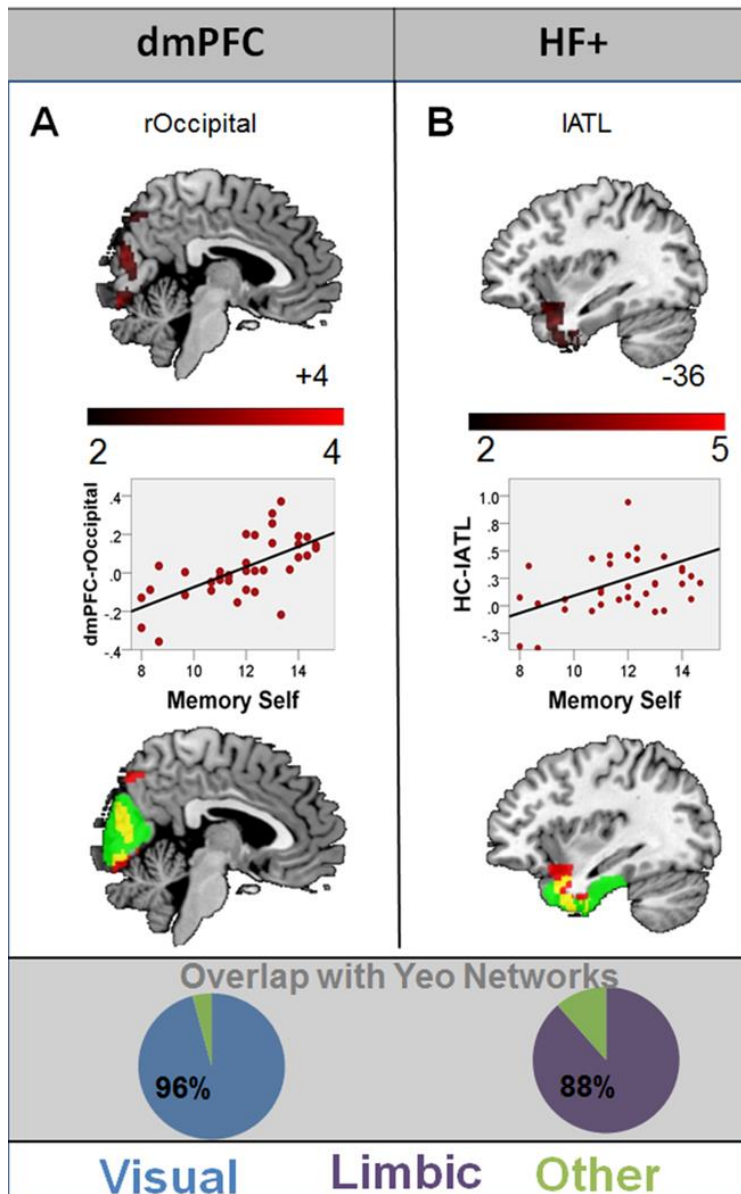


Figure 2.5: Functional connectivity (FC) of dorsomedial prefrontal cortex (dmPFC) and the hippocampal formation (HF+) associated with stronger memory for the self. A) Cluster in the right occipital with stronger FC to dmPFC for individuals with better memory for self-related items. B) Cluster in the left ventral Anterior Temporal Lobe (lvATL) with stronger coupling to HF+ for participants with better memory for items related to the self. First row: Cluster corrected maps illustrating regions of the FC map that correlate with behaviour. Second row: Scatterplot reflecting relationship between memory and FC between seed region and cluster. Third row: A) Overlap (yellow) between limbic Yeo network (green) and right occipital cluster (red). B) Overlap (yellow) between Yeo visual network (green) and IvATL cluster. Grey panel: Pie charts reflecting the percentage of the clusters that overlap with each Yeo network.

obtained for stronger memory for self-related items was associated with studies from the database containing terms such as retrieval, autobiographical, emotion, mentalizing, semantics and theory of mind. In contrast, connectivity maps obtained for better memory for best friend were associated with terms such as working memory, working and task. Importantly the term self-referential was positively associated with the maps obtained for self memory and negatively associated with those obtained for best friend memory. These patterns of associations are consistent with the proposal that the map associated with self-related memory is associated with relatively automatic processes, and ones that are characteristic of the DMN, while the map associated with memory for a best friend is associated with relatively controlled processes.

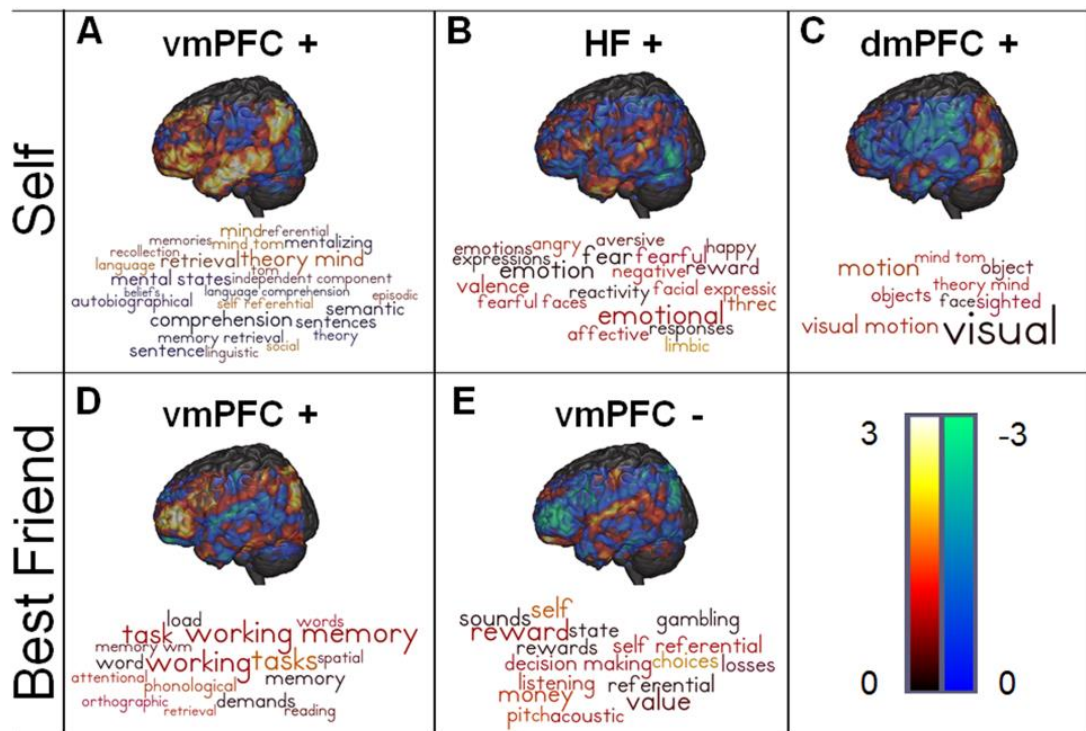


Figure 2.6: Neurosynth meta-analysis of the unthresholded images obtained for each significant contrast. A) Ventromedial Prefrontal Cortex (vmPFC) map B) Hippocampal formation (HF+) and C) Dorsomedial Prefrontal Cortex (dmPFC) maps associated with better memory for self-related items. D) vmPFC map associated with better memory for Best Friend (BF) related items. E) vmPFC map associated with worse memory for BF items.

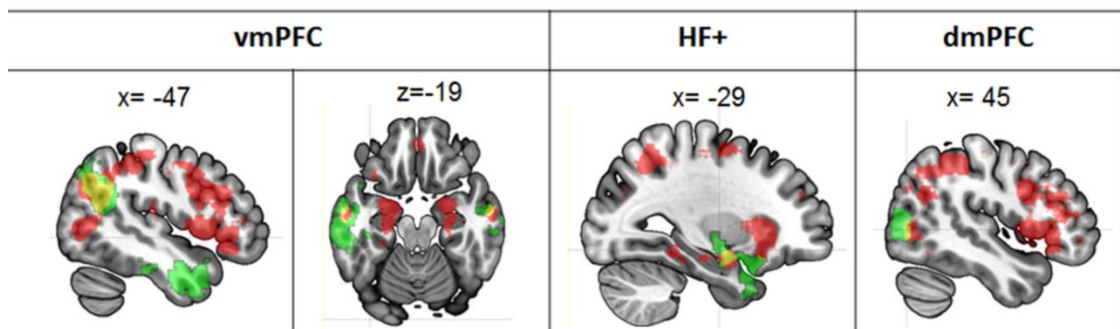


Figure 2.7: Overlap (yellow) between Neurosynth meta-analytic map for term self (red) and clusters predictive of memory for self items (green). First row represents the seed region from where the clusters in green were originated.

2.4.4. Neurosynth “Self” Map Activations

Finally, we formally compared the data produced through the individual difference analysis of resting-state functional connectivity approaches with a spatial meta-

analysis of peak activations performed by Neurosynth (search term: “self”; 903 contributing studies; <http://neurosynth.org/analyses/terms/self/>). The overlap between the meta-analytical map and the patterns of functional connectivity can be observed in Figure 7. It can be seen that there is overlap in several regions, most clearly in the left angular gyrus, and bilaterally in the lateral temporal lobe.

2.4. Discussion

The current study set out to understand whether the functional architecture of the mPFC and the HF+ at rest predicted the strength of incidental memories produced when personality adjectives were related in terms of their applicability to different agents. Consistent with previous studies (Kuiper & Rogers, 1979; Kelley et al., 2002), the magnitude of incidental memory effects was related to the personal relevance of the individual to which a trait adjective was rated: Stronger memories were formed for words related to the self than a best friend and the weakest memories were produced when words were rated with respect to David Cameron (a non-familiar control), the latter not surpassing chance performance. Using the scores for each referent as regressors in an individual difference analysis of resting-state functional connectivity, we found that stronger memories following self-related processing were related to stronger functional coupling between the vmPFC and bilateral mid temporal lobe, and left angular gyrus, as well as coupling between HF+ and regions of lvATL. We also found that stronger memory for self related items was linked to coupling between the dmPFC seed and a region of medial visual cortex, a region that falls at the boundary of the DMN and the visual cortex. In contrast, successful retrieval of words encoded with respect to the best friend was linked to decoupling between the ventral prefrontal cortex and the paracingulate gyrus, plus coupling with lateral parietal and prefrontal regions. No patterns of functional connectivity predicted memory scores for items related to David Cameron possibly due to retrieval for these items being at chance. Finally, a meta-analytic decoding of the connectivity maps predictive of self and best friend memory supported our distinction between individuals who excel at memory for themselves, rather than their best friends: Memory for self was associated with terms such as theory of mind, autobiographical or self-referential

Table 2.1

Regions that exhibited stronger functional coupling with the ROI dependent upon memory for either the self or other

Seed	MNI	Contrast	Cluster	Regions	Peak	Size	p-value	
vmPFC	0,26,-18	Self up	rMTG	Right medial temporal gyrus	62,-30,-12	641	0.0202	
			lAG	Left superior angular gyrus	-46,-54,26	1119	0.00071	
				Left superior LOC				
dmpFC	0,52,26	Self up	BF up	lMTG	Left medial temporal gyrus	-62,-28,-4	1951	5.6 E-6
					Left anterior temporal lobe			
			BF down	lMFG	Left medial frontal gyrus	-46,20,30	717	0.0114
				rSMG	Right superior SMG	22,-76,54	1029	0.00128
				rMFG	Right medial frontal gyrus	46,8,16	1111	0.000751
		Right inferior frontal gyrus						
		Paracingulate gyrus	Paracingulate gyrus	2,56,-2	1722	1.9 E-5		
HF+	-22,-20,-26	Self up	rOcc	Right lingual gyrus	30,-70,-16	1453	0.000242	
				Right supracalcarine gyrus				
				Right LOC				
		Self UP	lVATL	Left ventral ATL	-16,6,-20	1215	0.0006	

Note: Coordinates are based on the Montreal Neurological Institute coordinate system

AG: Angular Gyrus; BF: Best Friend; HF+: Hippocampal Formation; l: left; LOC: Lateral Occipital Cortex; MFG: Medial Frontal Gyrus; MTG: Medial Temporal Gyrus; OCC: Occipital; r: right; SMG: Supramarginal Gyrus; VATL: Ventral Anterior Temporal Lobe; vmPFC: Ventromedial Prefrontal Cortex

whereas enhanced memory for best friend was associated with terms like working memory.

It is often assumed that the reason why items that are referred to the self form strong memories is because of the rich associative structure that is associated with our knowledge of who we are (Symons & Johnson, 1997): this self-knowledge provides a strong schema to support memory encoding and retrieval allowing it to be retrieved efficiently and automatically. Prior work has shown that schema-based memory engages vmPFC (van Kesteren et al., 2010a; van Kesteren et al., 2012; Ghosh et al., 2014; McKenzie et al., 2014; Spalding et al., 2015) and our study suggests that a strong bias to remembering information rated to ourselves depends on forming a network between this region and lateral and anterior regions of the temporal lobe and the angular gyrus – regions that together make up the DMN (Raichle et al., 2001; Raichle & Snyder, 2007). Functional studies often implicate the DMN in situations when information from memory is often retrieved effortlessly, such as making global semantic associations (Bar et al., 2007; Wirth et al., 2011) periods of spontaneous thought (Mason et al., 2007) and the process of self-reference itself (Gusnard et al., 2001; Macrae et al., 2004; Northoff et al., 2006). These are all states that can involve the automatic retrieval of information from memory. Behaviourally we observed that self-memory was correlated with relatively poor performance on the SSRT. The SSRT is a measure of inhibitory control and previous studies have shown that errors in response inhibition are linked to a lack of DMN deactivation (Li et al., 2007). Moreover, SSRT can be used to distinguish subjects with attention deficit hyperactivity disorder (ADHD) from normal controls (Sendereka et al., 2012). Previous research on ADHD has also revealed reduced DMN deactivations during complex tasks (Fassbender et al., 2009) supporting the notion that successful executive control requires DMN deactivation. In addition, high activity in the DMN precedes lapses in cognitively demanding tasks (Weissman et al., 2006). Altogether our results therefore are consistent with the idea that self-relevant memories are supported by integrated activity within the DMN, a state that promotes the automatic and elaborated processing of associative information from memory that can at times be hard to inhibit.

Information related to best friends was retrieved more effectively than for the David Cameron control items. However, this type of memory was associated with a different network of regions than those observed for strong memories of the self. Better memory for a best friend involved a network that spanned the lateral surface of parietal and frontal cortex, including middle frontal and inferior frontal gyrus and supramarginal gyrus. Overlap with the Yeo networks, revealed that although this network was anchored in the vmPFC, these regions are a part of the dorsal attention and Frontoparietal Control networks, large-scale systems that are often activated by attention-demanding tasks (Collette et al., 1999; Corbetta & Shulman, 2002; Duncan, 2010). Thus unlike a strong memory for the self, a tendency to remember items related to one's best friend was linked to a coupling between ventral regions of the mPFC and regions beyond the broader DMN that are involved in goal-directed attention. Studies have shown that the lateral prefrontal cortex, particularly the inferior frontal gyrus, often activates when participants make semantic decisions that are more difficult either because the meaning is ambiguous or because participants must make links between stimuli that are only weakly related together (Noonan et al., 2013). More generally, co-activation between the DMN and the lateral prefrontal cortex occurs when novel or complicated decisions have to be made based on memory such as during creativity (Beaty et al., 2014) or when we plan the future (Spreng et al., 2010). Together the enhanced retrieval for best friend relative to the David Cameron control, as well as a functional connectivity network anchored in the vmPFC seed, suggest that memory for the best friend is likely to also benefit from an elaborate schema, perhaps one that is similar to that of the self (e.g., Mitchell et al., 2005). Importantly, this similarity with the self may mean that an accurate memory for close personal acquaintances is not only hampered by the weaker traces formed at encoding but may also depend on overcoming interference from associations with self memories and requires regions outside of the DMN that may function to guide retrieval in the face of interference. This possibility is supported by previous research which has commonly found inferior and dorsolateral prefrontal gyri, regions predictive of best friend memory in this study, to be involved in working memory processes (Curtis & D'Esposito, 2003). This hypothesis should be examined in future studies.

One general implication of our results is that vmPFC may act as a hub whose functional connectivity determines how schematic information is represented in the cortex. As well as connections to other regions of the mPFC, it can be seen from Figure 2 that this region of cortex is connected to medial aspects of the temporal lobe, as well as other limbic regions. In topographical terms this region is therefore well placed to integrate affective and episodic information into the broader prefrontal cortex. Consistent with this view, our data shows that, across people, the nature of the patterns of connectivity it exhibits at rest has implications for aspects of social memory: A strong memory for self-relevant information was associated with greater integration within the DMN, whereas a stronger memory for best friend required integration with regions important for executive control. One implication of this view is that the vmPFC exhibits modes of cortical processing that reflect how different aspects of mnemonic and affective information dominate cognition. Although our current data are consistent with this hypothesis, it is impossible to infer whether these patterns exert their effect on memory during encoding or retrieval since the current study explored individual differences in resting-state functional connectivity rather than measuring online neural activity. Future studies exploring different patterns of functional connectivity during different types of social and non-social memory retrieval will help to address this question.

It is worth considering certain limitations with the current data. Our study shows that better memory for different referents is associated with distinct patterns of functional connectivity however, the current study is unable to decipher whether the different patterns of functional connectivity predictive of memory for self and best friend items are indeed capturing the processing differences in referents per se, or whether instead they are reflecting differences in general memory strength. Future studies using a control memory task matched in accuracy to the reference task but instead employing a different memory manipulation such as elaborative semantic encoding will be able to address this issue.

Regardless of these issues, our results suggest that information related to the self and to one's best friend is supported by different patterns of functional connectivity with the vmPFC. Whereas information exclusively related to the self relies

on integration between this region and the DMN, remembering information about a similar other, benefits from integration between the vmPFC and executive control regions. We argue that this occurs because there are different strengths of association for the different types of memory. Memories associated with a best friend have weaker associations than do self-related. Consequently, remembering information about a personally significant other will require additional executive control directed either to retrieve the weaker memory trace, or to correctly select the appropriate memory despite interference from the stronger, and often associated, memories about the self.

Importantly, the current study found a negative correlation between inhibitory control and an individual's self-bias, suggesting that reduced inhibitory control is related to one's tendency to engage in self-focused attention. This in turn promotes states of perceptual decoupling that hinder task performance when sustained attention on the external world is required. The following chapter explores this relationship in more detail by using a cross-sectional design aimed at revealing patterns of functional connectivity in the resting-state that underpin this relationship.

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Chapter 3 - Don't you forget about me: The Self-Reference Effect and its Relationship to Inhibitory Control.

3. 1 Abstract

Self-relevant material automatically triggers reallocation of attention, leading to states of perceptual decoupling and errors during tasks. Contrarily to this detrimental effect, self-referential processing has a positive effect on encoding, termed the self-reference effect (SRE). The current study hypothesised that individuals with a stronger SRE, measured using a self/other reference paradigm, would be less efficient at inhibitory control measured using a Go/No-Go task (GNG). The neural underpinnings of such relationship was explored using resting-state fMRI in a cross sectional design: Patterns of functional connectivity of inhibitory control regions were studied in relation to the magnitude of the SRE. Similarly, functional connectivity of regions involved in self-reference was explored in relation to inhibitory control scores. Behaviourally, analyses confirmed a trade-off between inhibitory control and the magnitude of the SRE. Neurally, stronger coupling between executive control regions and ventral striatum was related to a reduced SRE. Instead, good inhibitory control was related to stronger coupling between self-referential regions and the right inferior frontal gyrus located in the salience network. The meaning of these patterns of functional connectivity and the role they might play in suppressing self-relevant information is discussed.

3.2 Introduction

The DMN is characterised as a set of highly coupled regions that show deactivation when attention is externally oriented (Greicius, Krasnow, Reiss, Menon, 2003; Raichle et al., 2001) and activations when information from memory is being processed (Spreng, Mar & Kim, 2009). As such, it is highly active during periods of rest in which the mind is free of task. This default state is characterised by spontaneous and effortless generation of thoughts, colloquially termed mind wandering (Seli et al., 2018; Smallwood & Schooler, 2015). However, despite originally having been considered a task-negative network (Fox et al., 2005) further research revealed that tasks which recruit processes that are engaged during the mind wandering state, which are dependent on memory, also recruit the DMN, shifting the understanding of the processes carried out by this network from a task-negative one to a component process one. Examples of the processes the DMN is involved in are scene construction (Hassabis, Kumaran & Maguire, 2007; Hassabis & Maguire, 2007), mental time travel (Botzung, Denkova & Manning, 2008; Schacter, Addis & Buckner, 2007; Spreng et al., 2009), narrative comprehension (Mar, 2011) and social cognition (Iacoboni et al., 2004; Mar, 2011; Spreng & Grady, 2010; Spreng et al., 2009), a common characteristic to all being that they rely on retrieval of episodic and semantic memory. Of special interest to the current study, self-referential processing also engages the DMN. This was first demonstrated by Kelley and colleagues (2002) who found stronger activation in midline cortical regions of the DMN during processing of items in a self-referential manner than during a non-self referential condition. In addition, Macrae, Moran, Heatherton and Banfield (2004) found that encoding of items processed in a self-referential manner was related to stronger activation of the mPFC, a main hub of the DMN, and a meta-analysis performed by Northoff and colleagues (2006) further revealed that the role of these regions during self-reference applies to different domains (e.g., emotional, facial, memory, spatial). These self-referential thoughts are often concerned with the individual's personal goals, constituting a core component of mind-wandering and future planning (Fox & Christoff, 2018; Smallwood et al., 2011; Stawarczyk & D'argembeau, 2015).

In the presence of an immediate goal this self-referential mode of cognition needs to be suppressed as adequate performance of either internally or externally oriented tasks requires attention to be sustained on task-relevant information until the task's goal is achieved. During memory retrieval carried out by the DMN the system enters a state of perceptual decoupling by which external stimuli are not processed thoroughly. Evidence for this account comes from EEG studies in which cortical responses to targets and distractors were reduced when the participants reported higher levels of mind wandering (Smallwood, Beach, Schooler & Handy, 2008). Consistent with the view that DMN activity leads to perceptual decoupling several studies have found reduced DMN deactivation preceding lapses of attention and errors during tasks (Li, Yan, Bergquist & Sinha, 2007; Weissman, Roberts, Visscher & Woldorff, 2006). Further evidence comes from studies showing that activation in the posterior cingulate cortex, a main hub of the DMN, increases during successful retrieval as well as during unsuccessful episodic encoding (Daselaar et al., 2009; Huijbers et al., 2012) which relies on processing of external stimuli. Because the spontaneous occurrence of processes carried out by the DMN may reflect a shift towards a state of memory guided cognition, if not suppressed efficiently under situations when external task-based information should be prioritized, DMN activity can interfere with goal-directed behaviour. Hence, during encoding or goal-directed action towards the external world, recruitment of mechanisms capable of suppressing the DMN are fundamental.

Although contemporary theories suggest that DMN must be suppressed during tasks that require encoding of detailed external information, the precise mechanisms by which this modulation occurs remain unclear. Research on inhibitory control mechanisms has revealed a set of regions consistently engaged during interference-resolution tasks. In particular, Nee, Wager and Jonides (2007) conducted a meta-analysis of 47 studies using a peak density analysis and reported a distributed set of regions engaged across a range of inhibitory control tasks. It consisted primarily of dorsolateral prefrontal cortex (dlPFC), inferior frontal gyrus, anterior cingulate cortex, anterior insula and posterior parietal cortex. This set of regions closely overlap with the FPCN defined in the parcellation by Yeo and colleagues (2011). Importantly these

set of regions have also been found to be anticorrelated with the DMN during the resting-state (Chai, Castañón, Öngür & Whitfield-Gabrieli, 2012; Fox et al., 2005) pointing towards the oppositional quality of DMN-related spontaneous cognition and FPCN-related controlled cognition.

The current study aims to understand the potential mechanisms by which the DMN fails to be downregulated in instances when the context requires it. Smallwood and Andrews-Hanna (2013) argue for a *context-regulation hypothesis* based on studies that have shown that individuals with higher working memory report less instances of mind wandering during demanding tasks (Kane et al., 2007; Mcvay & Kane, 2009) whereas other studies have shown higher mind-wandering during low demanding tasks in individuals with high working memory (Levinson, Smallwood, & Davidson, 2012). These results suggest that executive processes such as working memory, anchored in the FPCN, play an important role in regulating the occurrence of mind wandering in a manner that is dependent on the context.

The strong resemblance between the DMN and tasks that require self-focused attention (D'argembeau et al., 2005; Gusnard, Akbudak, Shulman & Raichle, 2001), the high degree of self-relevant content recruited during mind wandering (Fox & Christoff, 2018; Smallwood et al., 2011; Stawarczyk & D'argembeau, 2015) and research revealing that self-relevant material has similar properties to salient perceptual stimuli (Humphreys & Sui, 2015; Humphreys & Sui, 2016; Sui, Lui, Mevorach & Humphreys, 2013) lead us to hypothesise that certain instances of lapses of attention might be due to a shift towards a mode of self-relevant information processing. During these instances self-related information is probably signalled as more salient than task-related stimuli, with the resulting compromise on task performance. If this was the case, due to the reallocation of resources away from the task, individuals with a higher self-bias may perform worse on tasks that require sustained attention, such as tasks that depend on inhibitory control.

In order to measure individual differences in self-bias we measured the magnitude of the self-reference effect, which refers to the mnemonic advantage that material processed in reference to the self has over other types of processing. Many studies have found a positive correlation between this measure and one's tendency

to analyse the self, as measured through self-consciousness questionnaires (Agatstein & Buchanan, 1984; Hull, Van Treuren, Ashford, Proppom & Andrus, 1988; Nasby, 1985; Turner, 1980), suggesting that the heightened activation of self-related information required to engage in private self-consciousness results in a stronger mnemonic advantage towards material processed by this system. Hence the magnitude of the self-reference effect could potentially be used as an objective measure of self-focussed attention tendencies, the logic being that subjects with a reduced memory exclusively for self-related items (i.e who maintain a good memory performance on the control condition) have a reduced tendency for self-focussed attention. Contrarily, highly self-focused individuals will present a heightened memory exclusively for self-related items. Using a self-other reference paradigm, a previous study by this group found that heightened incidental encoding for items in the self-condition was correlated with worse inhibitory control (de Caso, Poerio, Jefferies & Smallwood, 2017).

The current study aims to replicate this negative correlation between inhibitory control efficiency and the magnitude of the self-reference effect as well as to explore potential patterns of functional connectivity in the resting-state involved in this DMN-FPCN interaction. To do this, two behavioural measures, one for self-bias (the self-reference effect) and one for inhibitory control (a Go / No-Go task) were recorded. These were used to understand the neural basis of the hypothesised interference between self-focus and effective external goal directed attention. We employed a localiser in a subset of participants to identify regions important for both self-reference and inhibitory control. To select the DMN regions of interest involved in self-reference a self/other reference localiser task was ran inside the scanner and the DMN defined by Yeo and colleagues (2011) was constrained by the map obtained for self > other contrast in the localiser task. The same procedure was used to obtain an inhibitory control region of interest. Using a Go/No-Go localiser task, the map obtained for the No-Go > Go contrast was used to constrain the FPCN defined by Yeo and colleagues (2011). If the process of self-reference interacts with inhibitory control processes then the magnitude of the self-reference effect might predict the functional connectivity of regions involved in inhibitory control. Similarly, functional connectivity

of regions involved in self-reference might predict inhibitory control. By applying this cross-sectional design this study aims to decipher patterns of functional connectivity that underlie the relationship between inhibitory control and the magnitude of one's self-bias, informing the theory surrounding how control mechanisms regulate self-focussed attention.

3.3 Methods

3.3.1. Participants

A total of one hundred and thirty nine (89 females, Age=22.50, SD= 2.93 years) healthy right-handed participants completed a self/other reference paradigm outside the scanner. A subset of these subjects (N= 51 (31 females, Age =20.2, SD = 1.86 years)) was later re-invited to complete a Go/No-Go paradigm in order to obtain measures of their inhibitory control ability. Both these tasks were performed outside the fMRI scanner and resting-state fMRI data was collected for all of the participants. The behavioural z-scores obtained from both paradigms were used as regressors of interest in subsequent second level seed-based analyses.

In order to select regions of interest for our seed-based analyses two localiser scans were performed. 21 subjects (13 females, Age=20.7, SD = 2.32 years) performed the Go/No-Go task inside the scanner in order to obtain areas more engaged during the No-Go than Go trials. 33 subjects (16 females, Age = 20.2, SD= 2.35 years) completed a self/other reference localiser task in order to obtain areas more highly active during self-referential processing than other-referential processing.

Once our seed-based analyses were completed, the clusters obtained predictive of the behavioural scores were seeded in an independent data set and a conjunction analysis was performed using the functional connectivity group maps of each cluster in order to find common regions with functional connectivity involved in the relationship between self-reference and inhibitory control. A chart describing the flow of the whole experiment can be found in Figure 3.1.

In exchange for their participation all subjects received either monetary reward or course credits. Approval for this project was granted by the York Neuroimaging Centre (YNiC) Ethics Committee and was conducted in accordance with

the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.

3.3.2. Behavioural Procedure

3.3.2.1 Self/Other Reference Paradigm

The laboratory task measuring the self-reference memory advantage involved an evaluation and a retrieval phase displayed in the left panel of Figure 1. The evaluation phase consisted of two social conditions and one syllable count condition. In the social conditions participants were asked to make decisions about the association between adjectives and one of two referents ('Self' or 'Lady Gaga'). In the syllable condition, participants indicated via button press whether the word on screen had three or more syllables or whether it had less. Adjectives were presented sequentially on-screen and participants were required to indicate whether each adjective applied to a particular referent/ had three or more syllables by pressing 'Y' with the index finger of their right hand for 'yes' or 'N' with the index finger of their left hand for 'no'. All words were selected from a pool of normalised personality trait adjectives with meaningfulness and likeability ratings (Anderson, 1968). An equal amount of positive, negative and neutral adjectives (40 adjectives /valence) with the highest meaningfulness rating were selected for this experiment. For each participant, these 120 words were randomly divided into two lists of 60 adjectives. One list contained all the items involved during the encoding phase, the other list contained the items that would be used as foils during the retrieval phase. This first encoding-phase list was divided into three lists of 20 items, each of which was assigned to one of the three conditions (Self, Lady Gaga, Syllables). Finally, these condition-specific lists were subdivided into two 10-item lists, one list per experimental block.

During encoding, participants were presented with these lists in separate blocks in an ABCCBA order allowing us to control for order effects within each participant. We also counterbalanced the order in which each category was presented

across participants. Each block was preceded by a screen indicating the specific condition and each block started after the participants button press. Stimuli were separated by an inter-stimulus interval of 5000ms during which participants were shown a blank screen with a fixation cross. Following the evaluation phase, participants were presented with a surprise retrieval test in which they were sequentially shown words and asked whether or not that particular item had been presented in the previous phase. This retrieval phase contained all the words from the previous stage of the experiment, plus an equal number of new words contained in the retrieval list. Items were presented in a random order and participants had to either press 'O' for old if they thought the word had appeared before or 'N' for new if they thought it was a new word. The old/new responses judged as "old" were followed by a source localisation judgement in which participants had to indicate using arrow heads whether they thought the old word had been presented during the self, the Lady Gaga or the syllable-count condition. Confidence ratings ranging from 1 (not confident at all) to 6 (very confident) for each old/new and source localisation judgements were also obtained. This paradigm allowed for 12 types of response types. Hits are considered old words that were correctly identified as old and correctly localised during the source localisation phase. This results in either "Self hits", "Lady Gaga hits" or "syllable hits". Old words judged as new would be considered misses, again resulting in either a "self miss", a "Lady Gaga miss" or a "syllables miss". New words judged as new were considered "correct rejections", and new words judged as old were considered "false alarms". Based on the incorrect source localisation of these new words, these can further be subdivided into "Self false alarms", "Lady Gaga false alarms" or "syllable false alarms". The false alarms scores specific to each referent allowed us to control for guessing at a referent specific level by subtracting them from the hits. Lastly, if an old word from, for example, the syllable condition was judged as old but then incorrectly source localised as Lady Gaga it was considered a "wrong source localisation from syllables to Lady Gaga condition".

Due to the effect familiarity can have on memory (Bower & Gilligan, 1979; Kuiper & Rogers, 1979; Kuiper, 1982), at the end of the experiment participants were asked to rate, on a scale of 1 to 6, their familiarity to Lady Gaga. Bivariate correlations ($r=.197$,

$p = .167$ revealed an insignificant effect of familiarity ratings on Lady Gaga memory, hence the original Lady Gaga memory scores were used in all analyses.

3.3.2.2. Go/No-Go Paradigm(GNG)

The GNG paradigm used in the current study originally had four different conditions. Two of them were semantic and the other two perceptual. The stimuli in the semantic conditions were either words or pictures, depending on condition, whereas the stimuli in the perceptual conditions were obtained by scrambling the stimuli from the semantic condition. The two perceptual conditions varied in difficulty. All stimuli were framed by a box that was slanted to different degrees (slight slant, medium slant or pronounced slant). Each trial consisted of a fixation cross, followed by the stimulus and the duration of the fixations and stimuli were jittered between 0.5-1s and 0.75-1.25s for fixation and stimulus respectively.

This task was originally developed to probe semantic inhibition (Alam, Murphy, Smallwood & Jefferies, 2018), however, in the current study we were only interested in performance during the hard-perceptual condition so will only describe this condition in detail. The stop-signal cue in the perceptual conditions was the degree of the slant in the framing box in such a way that participants had to withhold their response when the degree of the slant increased. In the hard-perceptual condition the slant between the Go and No-Go trials only varied slightly, from a slight slant to a medium slant, in contrast to the easy-perceptual condition in which the slant varied from slight slant to pronounced. The hard-perceptual GNG task is displayed in the right panel of Figure 1 and further details of this task, including stimuli generation, can be found in Alam et al. (2018).

3.3.3 Neuroimaging Procedure

3.3.3.1. Localiser Scans

3.3.3.1.1. Self/Other Reference Localiser

In order to obtain brain regions involved in self-reference 33 subjects performed a localiser scan inside the scanner. Similar to the encoding phase of the self-other reference paradigm described above, participants were presented with adjectives on the screen and depending on the experimental condition had to decide whether the adjective defined themselves (self-reference condition) or whether the adjective defined Barack Obama (control condition). A total of 30 neutral adjectives of similar word length were selected from a set of norms (Anderson, 1968) and two 15-item lists were created, counterbalancing across participants the condition for each list. For each trial the experimental condition was indicated by either the word “MYSELF” or “OTHER” and just above it the target word was presented in lowercase.

3.3.3.1.2. Go/No-Go Localiser Scan

The same Go/No-Go task used to obtain behavioural performance was used in the scanner to obtain regions more active during the No-Go trials than during the Go trials.

3.3.3.1.3. MRI Acquisition

For both localiser scans structural and functional data were acquired using a 3T GE HDx Excite MRI scanner with an 8-channel phased array head coil (GE) tuned to 127.4 MHz, at the York Neuroimaging Centre. Structural MRI acquisition was based on a T1-weighted 3D fast spoiled gradient echo sequence (TR = 7.8 s, TE = min full, flip angle = 20°, matrix size = 256 x 256, 176 slices, voxel size = 1.13 x 1.13 x 1 mm). Functional data was recorded using single shot 2D gradient-echo-planar imaging (TR = 3 s, TE = minimum full, flip angle = 90°, matrix size = 64 x 64, 60 slices, voxel size = 3 x 3 x 3 mm³, 180 volumes). A FLAIR scan with the same orientation as the functional scans was collected to improve co-registration between scans.

3.3.3.1.4. fMRI Analysis

For both localiser scans functional and structural data were pre-processed and analysed using FMRIB's Software Library (FSL version 4.1, <http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FEAT/>) (Smith et al., 2004). Individual FLAIR and T1 weighted structural brain images were extracted using BET (Brain Extraction Tool, Smith, 2002). Structural images were registered to the MNI-152 template using FMRIB's Linear Image Registration Tool (Jenkinson & Smith, 2001; Jenkinson, Bannister, Brady & Smith, 2002). The functional data were pre-processed and analysed using the FMRI Expert Analysis Tool (FEAT). Individual subject analysis involved: motion correction using MCFLIRT (Jenkinson et al., 2002); slice-timing correction using Fourier space time-series phase-shifting; spatial smoothing using a Gaussian kernel of FWHM 6mm; grand-mean intensity normalisation of the entire 4D dataset by a single multiplicative factor; highpass temporal filtering (Gaussian weighted least-squares straight line fitting, with $\sigma = 100$ s); Gaussian lowpass temporal filtering, with $\sigma = 2.8$ s.

For the self/other localiser scan first level analyses modelled the two experimental conditions (i.e self and other). Explanatory variables (EV) modelled time periods of each condition. For the Go/No-Go localiser scan first level analyses modelled 10 EVs, only two of them being of interest to the current study: the Go and No-Go time periods of the hard-perceptual condition. Z stat maps were generated for each EV; Self-reference and Other-reference as well as hard-perceptual No-Go and hard-perceptual Go trials. These maps were then registered to a high resolution T1-anatomical image and then onto the standard MNI brain (ICBM152). For both localiser scans, first level effects were entered into a group analysis using a mixed-effects design (FLAME, <http://www.fmrib.ox.ac.uk/fsl>) with automatic outlier detection (Beckmann, Jenkinson & Smith, 2003). The group analysis for the self-reference localiser included a self > other contrast and the group analysis for the inhibitory control included a No-Go > Go. Whole brain analyses were cluster corrected using a z statistic threshold of 3.1 (Eklund, Nichols & Knutsson, 2016) to define contiguous clusters. We controlled the rate of multiple comparisons using Gaussian Random Field Theory at a threshold of $p < .05$ (49).

3.3.3.2. Resting-state

3.3.3.2.1. Scan Acquisition

Functional MRI data was acquired on a 3 Tesla GE scanner. Participants observed a fixation cross for a scan that lasted 9 minutes. The scan had a repetition time of 2 seconds, resulting in 210 volumes. We used interleaved slice-timing and isotropic voxel dimensions of 3 mm³ (matrix size of 64 X 64, 192mm field of view, and 32 slices) with a 0.5mm gap between slices.

3.3.3.2.2. Pre-processing

All fMRI pre-processing and analysis was performed using FSL. We extracted the brain from the skull using the BET toolbox for both the flair and the structural T1 weighted images and these scans were registered to standard MNI152 (2mm) space using FLIRT (Jenkinson & Smith, 2001). Prior to conducting the functional connectivity analysis, the following pre-statistics processing was applied to the resting-state data; motion correction using MCFLIRT (Jenkinson et al., 2002); slice-timing correction using Fourier-space time-series phase-shifting; non-brain removal using BET (Smith, 2002); spatial smoothing using a Gaussian kernel of FWHM 6mm; grand-mean intensity normalisation of the entire 4D dataset by a single multiplicative factor; highpass temporal filtering (Gaussian-weighted least-squares straight line fitting, with sigma = 100 s; Gaussian lowpass temporal filtering, with sigma = 2.8s.).

3.3.3.2.3. First Level Analysis

Following these steps, the time series of 2 masks of interest were extracted. One of this masks represented the region of interest related to self-referential processing and was obtained by constraining the DMN as defined by Yeo and colleagues (2011) to the regions related to self-referential processing obtained in self>other contrast applied to the self/other localiser scan. The resulting mask can be visualised in bottom row of the top panel in Figure 3.3. The second mask contained regions involved in inhibitory control and was obtained by constraining the FPCN as defined by Yeo and colleagues (2011) to the regions related to inhibitory control

obtained in the No-Go > Go contrast applied to the Go/No-Go localiser. This mask can be visualised in the bottom row of the bottom panel in Figure 3.3.

The time series for each voxel within each mask were averaged and used as an explanatory variable in a subject-level functional connectivity analysis, which also included the following nuisance regressors: the first five principal time-series components extracted from white matter (WM) and cerebrospinal fluid (CSF) masks in accordance with the CompCor method (Behzadi, Restom, Liau & Liu, 2007) and six motion parameters. The Yeo et al (2011) parcellations in non-linear MNI152 volume space were downloaded from https://surfer.nmr.mgh.harvard.edu/fswiki/CorticalParcellation_Yeo2011 and resampled from 1mm³ to 2mm³. WM and CSF masks were generated by segmenting each individual's high-resolution structural image (using FAST in FSL). The default tissue probability maps, referred to as Prior Probability Maps (PPM), were registered to each individual's high-resolution structural image (T1 space) and the overlap between these PPM and the corresponding CSF and WM maps was identified. Finally, these maps were thresholded (40% for the SCF and 66% for the WM), binarised and combined. The six motion parameters were calculated in the motion-correction step during pre-processing. Linear displacements in each of the three Cartesian directions (x, y, z) and rotations around three axes (pitch, yaw, roll) were included for each individual. No global signal regression was performed (Murphy, Birn, Handwerker, Jones & Bandettini, 2009).

3.3.3.2.4. Second Level Analysis.

To understand whether the magnitude of the self-reference effect and inhibitory control scores varied with the functional connectivity of the areas involved in inhibitory control and self-referential processing, respectively, we used FSL to conduct two group-level regression of the connectivity matrices of each mask.

The first analysis examined whether the functional connectivity of regions involved in inhibitory control could predict the magnitude of the self-reference effect. We included the z-scores for the memory scores obtained for the self-referential and

the other-referential conditions as regressors of interest and were interested in the contrasts 1) Self Down and 2) Self Down, Lady Gaga up. The second analysis looked at whether the functional connectivity of the mask related to self-reference could predict the inhibitory control scores. In this analysis, we included the efficiency z-scores obtained from the GNG as regressor of interest. This technique allows us to examine regions within or outside the masks whose connectivity varies with particular traits (the magnitude of the self-reference effect and the inhibitory control scores respectively).

In order to control for spurious correlations related to subject motion we included framewise displacement as a regressor of no interest in both analyses (Power, Barnes, Snyder, Schlaggar & Petersen, 2012) and automatic outlier detection was selected in seed-based analyses. See Sormaz et al., (2017) for a prior demonstration of this approach. In these analyses the data were processed using FEAT version 5.98 part of FSL (FMRIB's Software Library, www.fmrib.ox.ac.uk/fsl) and the analyses were carried out using FMRIB's Local Analysis of Mixed Effects (FLAME). A grey matter mask with a probability threshold of 40% was used as a pre-thresholding mask and the cluster-forming threshold was set as z-score of 2.3. For these analyses we controlled for Type I errors by controlling for the number of voxels in the brain (Worsley, 2001), as well as the two tailed nature of our comparisons yielding an alpha value of $p < .025$ FWE.

3.3.3.3 Conjunction Analysis

Once the group level regression analyses were finalised the cluster obtained for the Self Up, Lady Gaga up contrast and the cluster involved in better inhibitory control were both independently seeded in a new data set (N=59) with the same MRI Acquisition, pre-processing and analysis parameters as the other data set. With the aim of finding regions simultaneously related to better inhibitory control and reduced self-reference effect a formal conjunction analysis using FSL's "easythresh-conj" tool was performed (Nichols, Brett, Andersson, Wager & Poline, 2015).

3.3.3.4. Neurosynth Meta-analyses

In order to study how clusters obtained in this study were related to previous neuroimaging studies, meta-analyses were performed using the online Neurosynth database (Yarkoni, Poldrack, Nichols, Van Essen & Wagner, 2011). In particular, we performed a meta-analytic decoding of 1) the unthresholded functional connectivity group map of the cluster obtained in the FPCN seed-based analysis predictive of memory of reduced self-reference effect, 2) the unthresholded functional connectivity group map of the cluster obtained in the DMN seed-based analysis predictive of inhibitory control efficiency, 3) the unthresholded functional connectivity group map of the mask obtained in the conjunction analysis. This was done by uploading the corresponding unthresholded maps onto Neurosynth and performing a cognitive decoding of each map. This function allows the identification of cognitive terms in the database that are most strongly associated with the uploaded map. The results of these terms are displayed in the form of word clouds in the relevant figures.

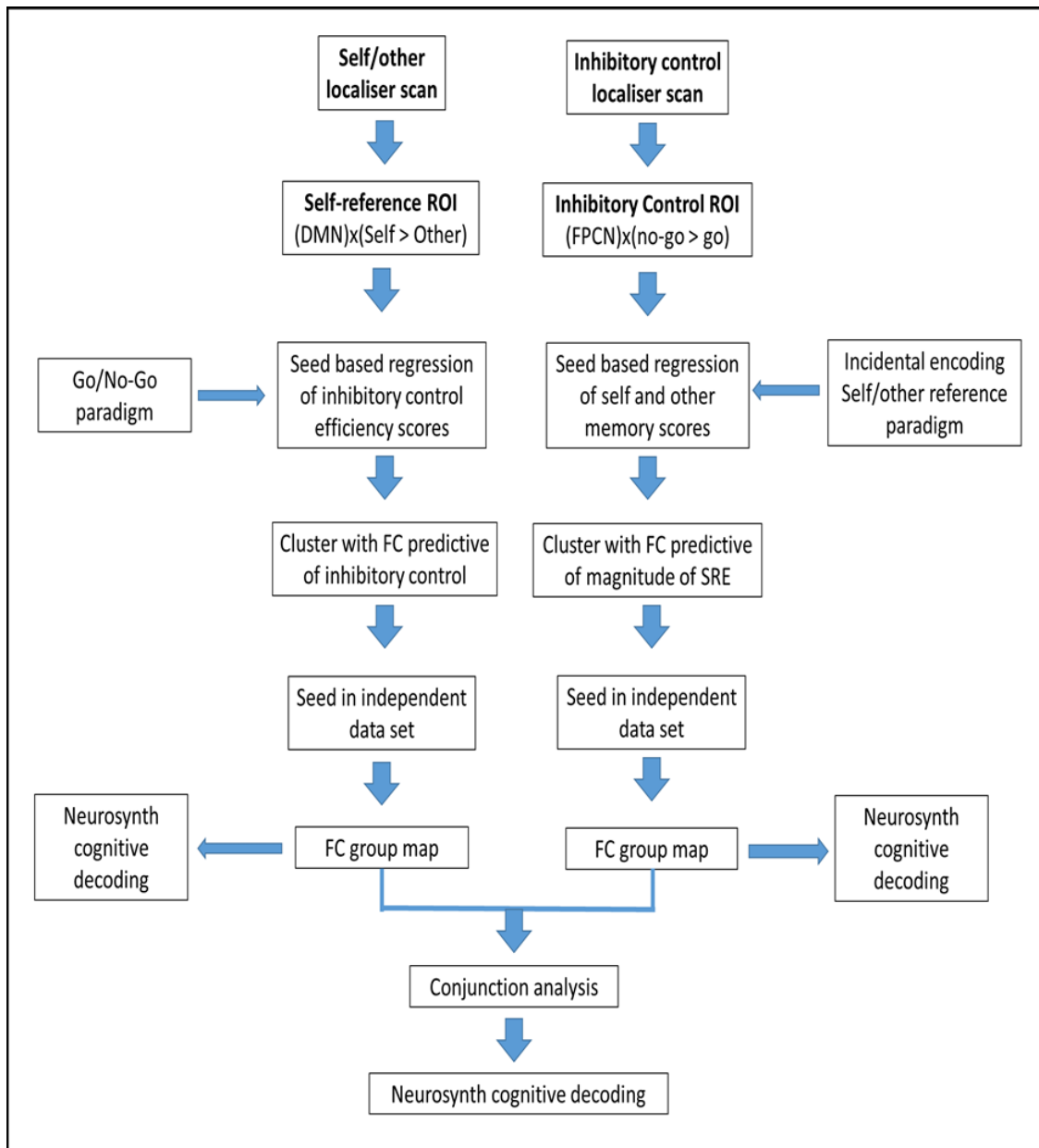


Figure 3.1 : Flow chart describing all the steps performed in the current study. Two localiser scans were performed to select regions of interest for inhibitory control and self-referential processing. Behavioural scores for both paradigms were collected outside of the scanner and used as regressors in the seed-based analyses using a cross-sectional design. The clusters obtained in the seed-based regressions were seeded in an independent data set and the functional connectivity group maps used in a conjunction analysis. Meta-analytic decoding was performed on the functional connectivity group maps and the conjunction map in order to obtain cognitive terms in Neurosynth database related to each map.

3.4 Results

The current study aimed to study the relationship between inhibitory control efficiency and the degree of self-bias as well as to explore patterns of functional connectivity underpinning such relationship. In order to calculate an individual's self-bias their memory for items processed in a control condition, namely in relation to Lady Gaga, were subtracted from the memory scores obtained for items processed in reference to the self, obtaining a measure of the magnitude of their self-reference effect. Efficiency scores from a Go/No-Go paradigm were used as a measure of inhibitory control and the relationship between the behavioural scores obtained in each paradigm was analysed using a hierarchical regression analysis.

To explore patterns of functional connectivity involved in the relationship between mnemonic advantage for self-related items and inhibitory control these behavioural measures were used to drive seed-based regression analyses using a behavioural-resting-state functional connectivity cross-sectional design. In particular, the memory scores related to the mnemonic advantage of self-related items were used to predict functional connectivity of regions involved in inhibitory control, whereas performance scores at the GNG task were used to predict patterns of functional connectivity of regions involved in self-referential processing. The regions of interest were selected through running localiser tasks for self-reference and inhibitory control and using the maps obtained for self > other and No-Go > Go to constrain the DMN and FPCN as defined by Yeo and colleagues (2011), respectively.

Lastly, the clusters with functional connectivity predictive of behaviour obtained in our seed-based analyses were seeded in an independent data set to obtain their functional connectivity group maps and a conjunction analysis of these functional connectivity group maps was performed to extract regions that potentially coordinate the patterns of functional connectivity predictive of behaviour.

The maps obtained for the localiser scans, the seed-based regressions and the functional connectivity of the cluster obtained, as well as the conjunction analysis of said functional connectivity group maps can be found in the following link: <https://neurovault.org/collections/3904/>.

3.4.1 Behavioural Results

3.4.1.1. *Self–Reference Effect*

Memory scores for each referent were calculated by counting how many words from each condition were source localised correctly. In order to control for guessing the number of new words erroneously assigned to each referent (false alarms) was subtracted from the number of correctly source localised words. In particular, the proportion of new words erroneously assigned to, for example, the syllable condition was subtracted from the proportion of old syllable-count words that were correctly source localised. This was done for the 3 conditions. The memory for each referent is presented in the bar graph in Figure 3.2.

A repeated measures analysis of variance (ANOVA) was conducted using the data from the 139 participants who completed the self-reference task. The three memory measures were included as a within-subject factor ($F(2,276) = 394.4$, $p < .0001$, $\eta^2 = .741$) revealing a significant effect of condition on memory scores. Paired sample t-test revealed the expected mnemonic advantage of self-related material over both the Lady Gaga condition ($t(138) = 12.6$, $p < .0001$, $d = 1.07$) and the syllable count condition ($t(138) = 28$, $p < .0001$, $d = 2.38$). The memory scores between the 2 control conditions were also significantly different $t(138) = 15.1$, $p < .0001$, $d = 1.28$) with Lady Gaga scores being significantly higher than syllable count scores. Figure 3.2 shows these differences in memory performance across the 3 conditions.

We repeated this analysis using only the subjects that completed the GNG task ($N=51$) to assure these results were consistent in our subsample. A significant effect of condition was again found ($F(2,100) = 106.9$, $p < .0001$, $\eta^2 = .681$) with memory for Lady Gaga being significantly higher than memory for syllables ($t(50) = 7.9$, $p < .0001$, $d = 1.12$) and memory for self-related items being significantly higher than memory for Lady Gaga items ($t(50) = 6.9$, $p < .0001$, $d = .97$). Hence our results replicate the well-established mnemonic advantage that material processed in relation to the self holds. In both samples memory for syllables was not above chance performance (Full sample:

N=139, Mean = .32, SD = .17; Subsample N= 51, Mean = .33, SD = .2) and was therefore excluded from the subsequent behavioural and resting-state analyses.

3.4.1.2. Go/No-Go Paradigm

Inhibitory control efficiency scores were calculated by dividing the response time at Go trials (when a response was required) by the accuracy on the No-Go trials (when a response was successfully repressed), RT = 0.5s, SD = .07; Accuracy = 70.22%, SD = 17.87. Note that lower efficiency scores therefore represent better performance at the GNG task (Mean efficiency scores = .81, SD =.37). Five outliers were detected, all performing below 3 standard deviations from the mean. The scores of these participants were imputed to 2 standard deviations of the mean and these efficiency scores were used for further analyses (Mean efficiency scores after imputing for outliers = .78, SD = .3).

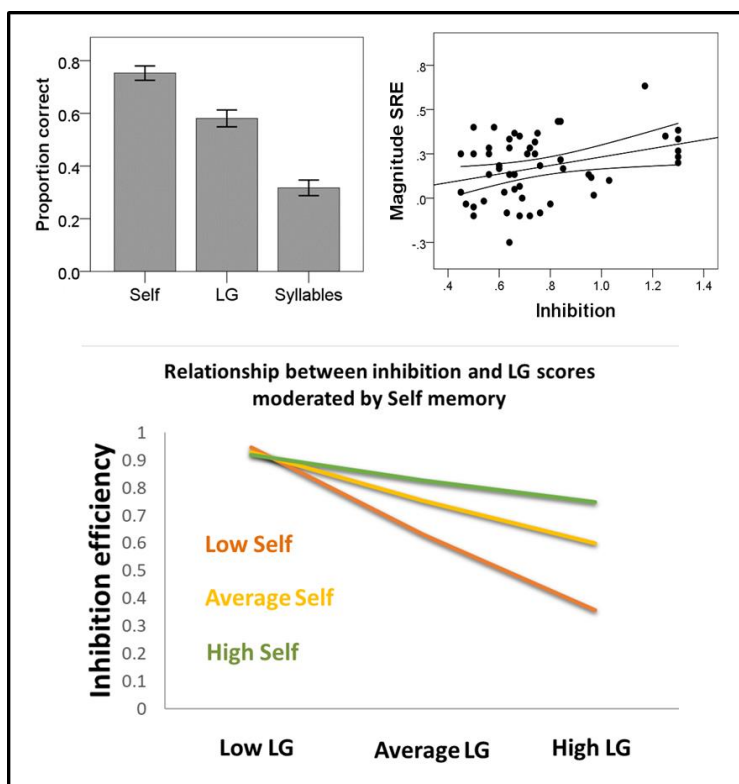


Figure 3.2: Behavioural results. Top Left: Bar graph displaying memory scores for each condition after controlling for guessing by subtracting number of false alarms in each condition. Top Right: Scatterplot displaying the correlation between the SRE and inhibitory control (high values reflect worse efficiency). Bottom: Interaction plot displaying the relationship between inhibitory control and memory for Lady Gaga items moderated by memory for self-related items. At high levels of performance at the Lady Gaga condition the effect of self-bias on inhibition becomes apparent.

3.4.1.3. Relationship between the Self-Reference Effect and Inhibitory Control

For each control condition, the magnitude of the self-reference effect was calculated by subtracting the memory scores in either control condition from the memory scores in the self-referential condition. Next, bivariate correlations between these measures and the efficiency scores at the Go/No-Go task were carried out. A positive correlation was found when computing the self-reference effect by subtracting Lady Gaga memory scores from self-referential memory scores ($r = .316$, $p = .024$). Note that lower efficiency scores at the GNG represent better performance hence the positive correlation is reflecting that individuals with a stronger self-reference effect have worse inhibitory control. The relationship between the self-reference effect and inhibition is displayed visually in the scatterplot in Figure 3.2.

A linear regression was performed in order to identify whether the aspect of the self-reference effect linked to inhibitory control was a result of better memory for the self or worse memory for Lady Gaga, both of which would result in a reduced self-reference effect. Efficiency scores at the GNG were included as the dependent variable with the memory scores for Lady Gaga and self used as predictors. In addition, an interaction term between the two predictors was added in a hierarchical regression analysis. To avoid potentially problematic high multicollinearity with the interaction term, the variables were centred and an interaction term between self and Lady Gaga memory scores was created (Aiken & West, 1991). This interaction term accounted for a significant proportion of the variance in the inhibition efficiency scores ($\Delta R^2 = .067$, $\Delta F(1,47) = 4.22$, $p = 0.045$, $b = 2.27$, $t(47) = 2.03$, $p = .045$). There was also a main effect of Lady Gaga memory on inhibition scores ($B = -.78$, $t(47) = -3.2$, $p = .002$). Regarding the self-referential condition, there was a trend towards a significant effect ($B = .48$, $t(47) = 1.8$, $p = .076$).

To understand the interaction effect, the data was plotted and can be visualised in the line graph in Figure 3.2. This plot helps us distinguish individuals who have a low self-memory due to low overall memory, as measured through the low Lady Gaga memory score, from those whose low self-memory is not due to bad

encoding mechanisms (as inferred from their high Lady Gaga scores). From the line graph it can be seen that high performance at self-related memory has a detrimental effect on inhibition, and how this effect becomes apparent within subjects with high memory for the memory control condition (i.e, Lady Gaga items). In these subjects we can confirm that low scores for self are not due to a bad encoding/retrieval ability, as they present good memory in the Lady Gaga condition. Instead, the individuals with the best inhibitory control (lower scores) are not those with the best memory scores for both conditions, but those who, on top of having a good memory for the non-self control condition, have a reduced mnemonic advantage for self-related items. This strongly supports the idea that a mnemonic advantage for self-material is capturing an aspect of self-focussed attention that acts as a distractor, with low scores for self-related material accompanied by high memory for the control condition potentially reflecting a reduced tendency to focus attention towards the self.

3.4.2. Neuroimaging Results

3.4.2.1 Selection of Seed Regions

The aim of the study was to explore the neural mechanisms that describe the relationship between inhibitory control and one's tendency for self-reference (as measured through the magnitude of the self-reference effect). In particular, we wanted to know whether patterns of functional connectivity of areas activated in periods of self-reference relate to individual variations in inhibitory control, as well as whether patterns of functional connectivity of areas engaged during inhibitory control could predict the magnitude of one's memory advantage for self-related items.

Prior meta-analytic studies have shown that self-reference engages regions within the DMN (Northoff et al., 2006) whereas inhibitory control activates areas in the FPCN (Nee et al., 2007), making these networks seed region candidates for the functional connectivity behavioural regressions. To constrain the size of these regions of interest we ran two localiser tasks in subsets of our larger sample to identify aspects of these networks that are most relevant to the specific cognitive processes. A Go/No-

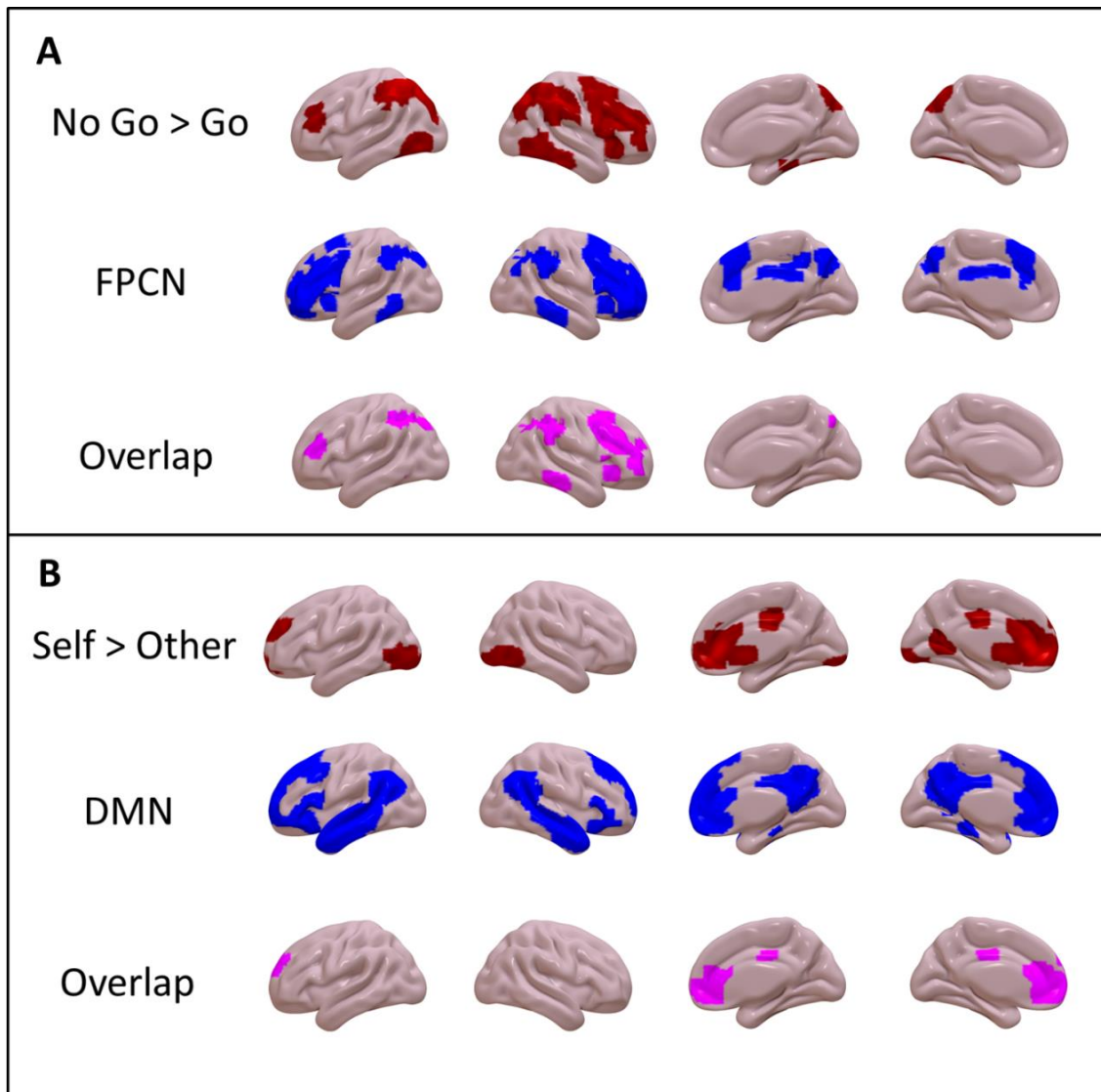


Figure 3.3: *Generation of regions of interest for the seed-based analyses.* A: Generation of seed region involved in inhibitory control. Top row displays the clusters obtained for No-Go > Go in the localiser scan. Middle row displays the Frontoparietal Control Network (FPCN) as defined by Yeo et al (2011). Bottom row displays the overlap between the FPCN and the areas obtained for No-Go > Go contrast. The relationship between the functional connectivity of this mask and the magnitude of the self-reference effect was explored in the first analysis. B: Generation of seed region involved in self-referential processing. Top row displays the clusters obtained for self > other in the localiser scan. Middle row displays the Default Mode Network (DMN) as defined by Yeo et al (2011). Bottom row displays the overlap between the DMN and the areas obtained for self > other contrast. The relationship between the functional connectivity of this mask and efficiency scores at inhibitory control was explored in the second analysis

Go task was performed to obtain regions engaged during inhibition (No-Go > Go, N = 21, see Methods). The comparison of No-Go > Go events revealed 6 clusters located in the right lateral prefrontal cortex, right and left superior parietal lobe, right occipitotemporal lobe, left occipital lobe and left frontal pole. More details about these clusters can be found in Table 1. In addition, a self/other reference task was also

scanned to obtain regions engaged during self-reference (N = 33, see Methods). Comparison of the process of self-reference with the control condition revealed 4 clusters located in the mPFC, the left and right occipital lobes and the posterior cingulate cortex. Further details can be found in Table 2. The No-Go > Go activation map, displayed in Figure 3.3A (top row) was then multiplied by the FPCN as defined by Yeo et al (2011) (Figure 3.3A, middle row) in order to obtain the final inhibitory control related mask (Figure 3.3A, bottom row). Similarly the map obtained for self > other displayed in Figure 3B (top row) was multiplied by the DMN (Figure 3.3B, middle row), using the resulting map as the self-reference mask (Figure 3.3B, bottom row) in the subsequent seed-based behavioural regressions of inhibition scores.

3.4.2.2. Seed-Based Behavioural Regressions

Having established regions of interest within DMN and FPCN that are sensitive to the process of self-reference and inhibition, respectively, we conducted two independent seed-based analyses with the aim of identifying whether the patterns of functional connectivity from regions of importance for inhibition were predictive of the magnitude of the self-reference effect and vice versa. A group regression was performed on the functional connectivity maps of the inhibitory control region of interest (Figure 3.3A, bottom row) using the scores from the self-reference task as regressors (memory scores from the syllable count condition were not included). This analysis included the 139 participants who completed the self-reference task. Results revealed a pattern of functional connectivity from the inhibitory control region to a subcortical cluster to be predictive of memory for self-related items. This cluster is displayed in green in the glass brain at the top left of Figure 3.4. In particular, stronger functional connectivity between the FPCN and this cluster was related to reduced memory scores in the self-referential condition, as can be seen from the green scatterplot. In addition, the contrast for Self Down, Lady Gaga up revealed a left-lateralized subsection of this cluster encompassing the left thalamus and left striatum. This cluster is displayed in yellow in the bottom glass brain as well as in the axial and sagittal slices of Figure 3.4 and, as can be seen from the yellow scatterplot, as the magnitude of the self-reference effect gets smaller so does the decoupling between

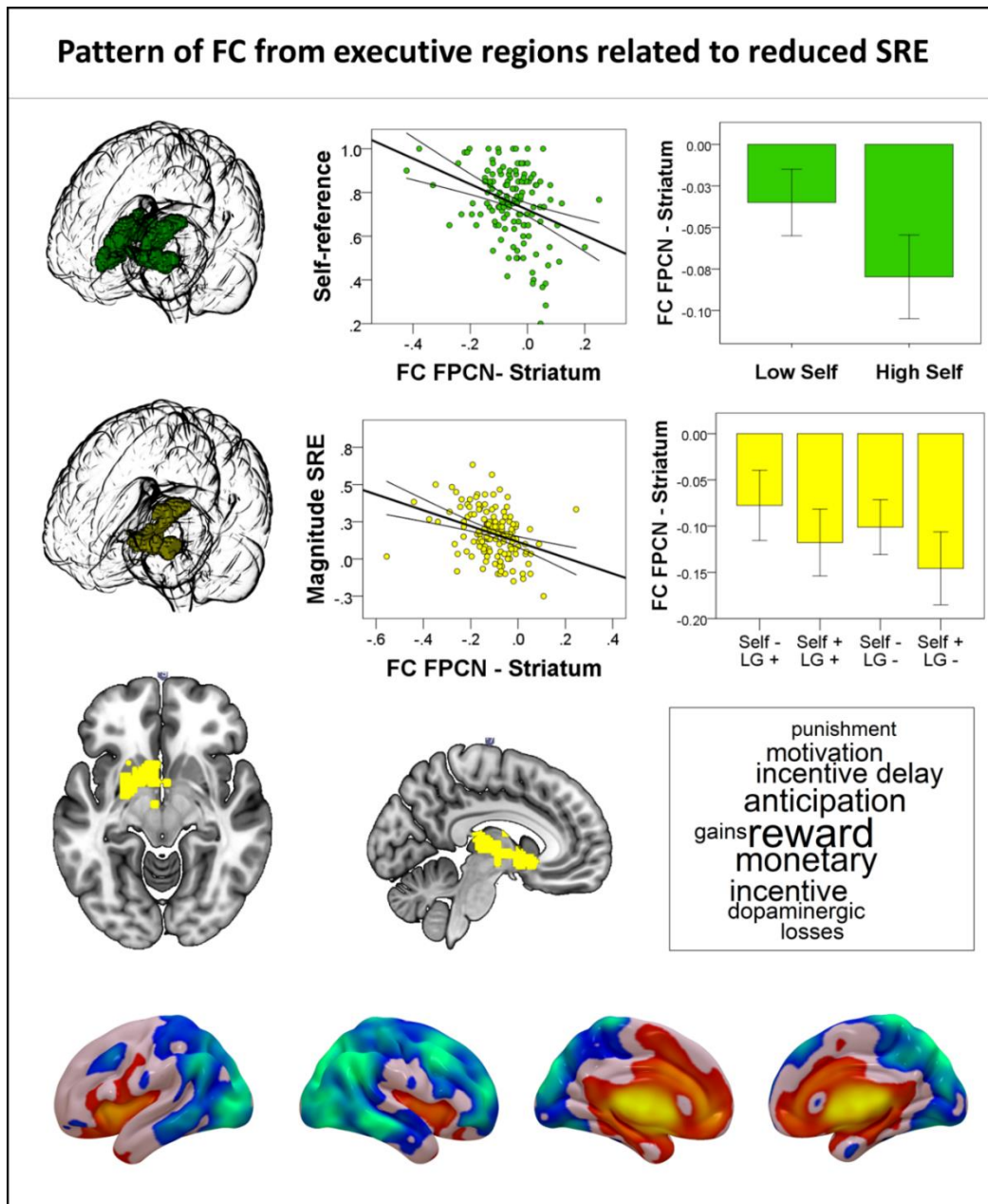


Figure 3.4: Relationship between the functional connectivity (FC) of inhibitory control related regions and the magnitude of the self-reference effect (SRE). The top glass brain displays the subcortical cluster (green) found to be more coupled to the inhibitory control related seed region in subjects with a reduced self-memory, whereas the bottom glass brain displays the subsection of the subcortical cluster (yellow) found to be more coupled to the inhibitory control related seed region in subjects with a reduced SRE. The scatterplots show these relationships: x axis displays the connectivity between the seed region and these cluster and the y axis displays the memory scores. Groups were generated by median splitting the memory scores and the mean FC of each group is displayed in the bar graphs. The subcortical cluster obtained for the SRE was further used as a seed region to explore its functionality. The inflated brains at the bottom display the FC group map of this cluster, with warm colours indicating areas that are functionally coupled above average to the subcortical cluster and blue indicating areas that are coupled below average. The word cloud on the bottom right displays the results from a meta-analytic cognitive decoding of the FC group map using Neurosynth.

Table 3.1

Clusters obtained for the No-Go > Go contrast using the inhibitory control localiser

Cluster location	Regions	Peak	Size	p-value
Right Lateral PFC	Frontal pole Middle frontal gyrus Frontal orbital cortex Insular cortex Inferior frontal gyrus pars opercularis Precentral gyrus Superior frontal gyrus	54, 14, 36	2589	1.75E-14
Right Superior Parietal Lobe	Supramarginal gyurs anterior division posterior division Angular gyrus Lateral occipital cortex superior division Superior parietal lobule	46, -42, 48	2233	4.39E-13
Left Superior Parietal Lobe	Supramarginal gyrus anterior division posterior division Lateral occipital cortex superior division Postcentral gyrus Superior parietal lobule	-38, -44, 42	1658	1.36E-10
Right occipitotemporal lobe	Inferior temporal gyrus posterior division temporooccipital part Lateral occipital cortex inferior division Middle temporal gyrus temporooccipital part	54, -34, -20	1417	1.82E-09
Left Occipital Lobe	Temporal Occipital Fusiform Cortex Lateral occipital cortex inferior division Inferior temporal gyrus temporooccipital part	-46, -72, -6	796	3.3E-06
Left Frontal Pole	Frontal pole	-42, -40, 20	245	0.02

Note: Coordinates are based on the Montreal Neurological Institute coordinate system. Regions are based on the Harvard-Oxford Cortical Structural Atlas

Pattern of FC from self-referential regions related to enhanced inhibition

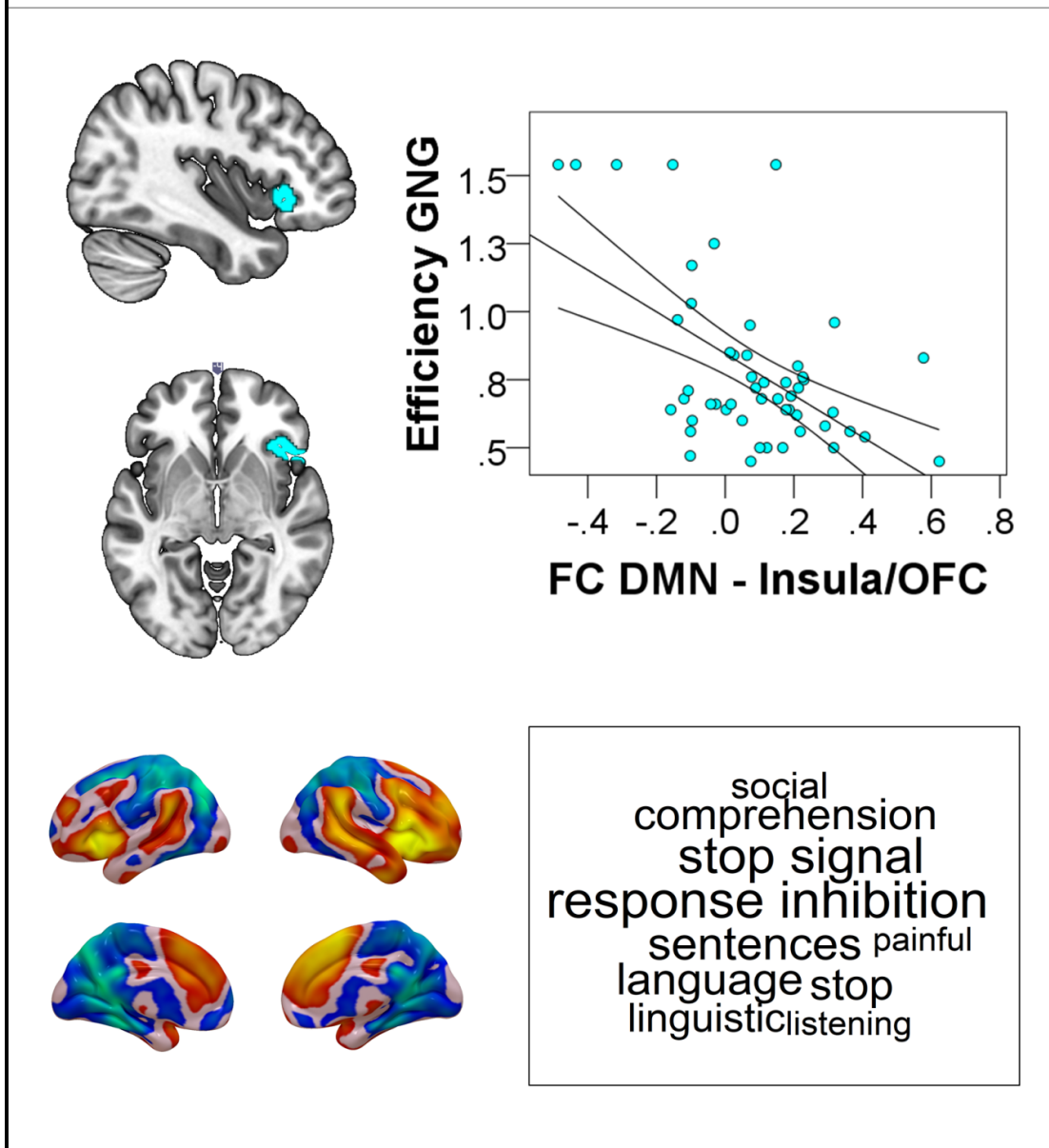


Figure 3.5: Relationship between the functional connectivity (FC) self-referential related regions and efficiency scores of the Go/No Paradigm. The sagittal and axial slices display the cluster (cyan) in the right insula/orbitofrontal cortex found to be more coupled to the self-referential related seed region in subjects with better efficiency scores at the Go/No-Go Paradigm (lower scores). The scatterplot shows this relationship with the x axis displaying the connectivity between the seed region and this cluster and the y axis displaying the efficiency scores of the Go/No-Go Paradigm. This cluster was further used as a seed region to explore its functionality. The inflated brains at the bottom left display the FC group map of this cluster, with warm colours indicating areas that are functionally coupled above average to the subcortical cluster and blue indicating areas that are coupled below average. The word cloud on the bottom right displays the results from a meta-analytic cognitive decoding of the FC group map using Neurosynth.

these regions. To visualise this effect, the sample was median split on the basis of their memory for self-items and Lady Gaga items, presented in Figure 3.4 in the form of a bar plot. For the yellow bar graph participants were then grouped in either of 4 groups based on their memory for self and Lady Gaga. The bar graphs display the mean functional connectivity in each group. It can be seen that the individuals with below median memory scores for the self-condition have the highest FPCN-striatal coupling. Note from the yellow bar graph that the magnitude of the coupling between FPCN and striatum is not informative of the memory in the control condition as not all individuals with a higher memory score for Lady Gaga have less or more functional connectivity than all individuals with reduced Lady Gaga memory, suggesting this pattern of functional connectivity is specifically related to the magnitude of the self-reference effect and not to overall encoding/retrieval mechanisms. Further details about these clusters can be found in Table 3. In order to assign a functional role to these subcortical clusters, we seeded the cluster obtained from Self Down, Lady Gaga up in an independent data set (see Methods) and performed a meta-analytic decoding of the connectivity map using Neurosynth (Yarkoni et al 2011). The functional connectivity group map of this subcortical cluster is displayed in the inflated brains at the bottom of Figure 3.4, along with a wordcloud containing the most associated cognitive terms. This analysis revealed terms such as “reward” and “anticipation”.

Having documented a relationship between regions important for controlled processing and variation in self memory, our next analysis considers the same question from the opposite perspective. Using a subset (N=51) of the larger sample that had measures of inhibitory control, we examined how this variable was linked to functional variation in regions linked to the process of self-reference. In this case the midline cortical areas engaged during self-reference displayed a pattern of increased temporal correlation to the right insula and right orbitofrontal cortex predictive of inhibitory control efficiency. In particular, stronger functional connectivity between the self-reference seed region and this cluster was predictive of better efficiency scores during the inhibition task. This relationship can be seen in the scatterplot in Figure 3.5, where the x-axis represents the functional connectivity between the seed region and the right insula/orbitofrontal cortex and the y-axis represents the

efficiency during inhibition (smaller values represent better performance). The brain slices in Figure 3.5 display the location of the cluster. See Table 4 for further details. This cluster was subsequently used as a seed region to obtain its functional connectivity group map, displayed in the inflated brains located at the bottom left of Figure 3.5. Cognitive decoding of this functional connectivity group map using Neurosynth revealed behavioural terms linked to inhibitory control such as “response inhibition” and “stop signal” as well as terms linked to language (word cloud in Figure 3.5).

After having found patterns of functional connectivity related to both of our behavioural measures we conducted a formal conjunction analysis between the functional connectivity group maps obtained from seeding each cluster to examine potential underlying intrinsic architecture common to both effects. This conjunction analysis revealed that the functional connectivity group map of the insula/orbitofrontal cortex cluster and the functional connectivity group map of the subcortical cluster overlapped in regions that included cortical, striatal and thalamic regions. These regions are displayed in the inflated brains in Figure 3.6 while the word cloud describes the results of a meta analytic decoding of this network using Neurosynth. The pie charts in Figure 3.6 display the overlap between the cluster and each cortical and striatal network as defined by Yeo et al (2011), as well as the overlap of the cluster with the thalamic nuclei found in FSL’s Oxford Thalamic Connectivity Probability Atlas. The thalamic nucleus most involved in the conjunction map found was the nucleus that projects into the prefrontal cortex. This nucleus is the dorsomedial thalamic nucleus previously associated with the salience network (Seeley et al., 2007). The striatal network that overlapped most with the conjunction map was the executive network whereas the cortical network that overlapped most with the conjunction map was the salience network. These results clearly suggest that the relationship between the self-reference effect and inhibitory control is driven by interactions between the FPCN, the DMN and the salience network.

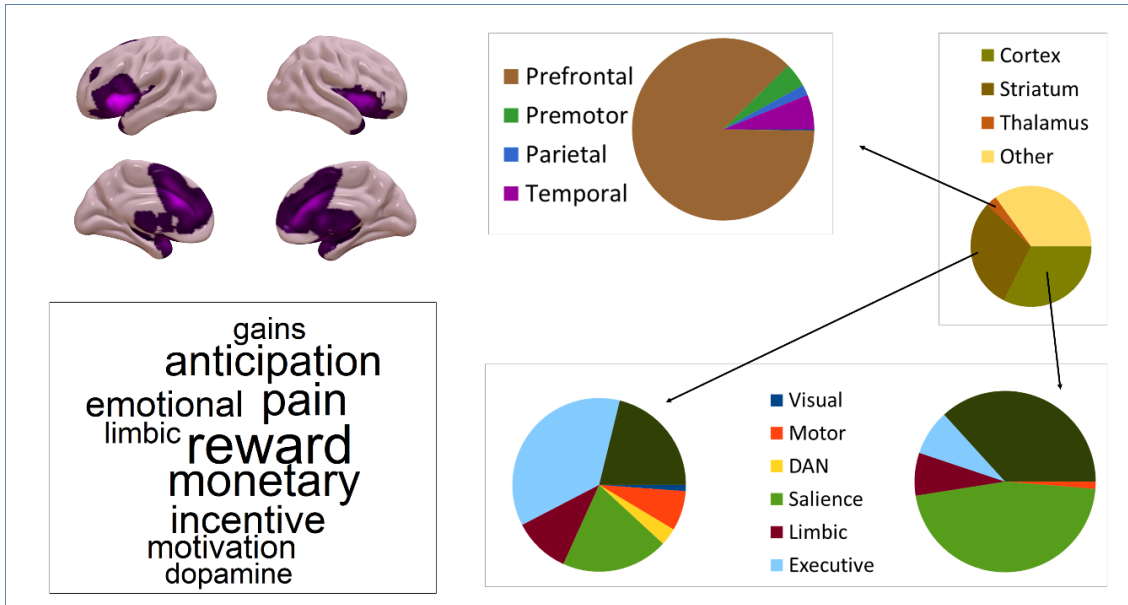


Figure 3.6: Conjunction analysis of the functional connectivity group maps obtained by seeding the subcortical and right insula clusters. The inflated brains display the conjunction map and the word cloud displays the results from a meta-analytic cognitive decoding of the conjunction map. The pie chart on the top right displays the proportion of the conjunction map that falls into cortical, striatal, thalamic or other (white matter) areas. The top left pie chart displays which thalamic nuclei (using FSL’s Oxford Thalamic Connectivity Probability Atlas) the conjunction map overlapped with. The bottom left pie chart displays the proportion of the cortical section of the conjunction map that overlaps with each of the cortical networks defined by Yeo et al (2011). Similarly, the bottom right pie chart displays the proportion of the striatal section of the conjunction map that overlaps with each of the striatal networks defined by Choi et al (2012).

Table 3.2

Clusters obtained for the self > other contrast using the self-referential localiser.

Cluster location	Regions	Peak	Size	p-value
Medial Prefrontal Cortex	Anterior cingulate cortex Paracingulate gyrus Subcallosal cortex Frontal medial cortex Frontal pole	0, 40, 0	2694	1.78E-11
Left Occipital Lobe	Occipital pole Occipital fusiform gyrus Lateral occipital cortex inferior division Precuneus Intracalcarine cortex	-22, - 52, 6	1704	2.09E-08
Right Occipital Lobe	Occipital pole Occipital fusiform gyrus Lateral occipital cortex inferior division	20, -88, -14	1002	7.6E-06
Posterior Cingulate Cortex	Posterior cingulate cortex	-2, -18, 32	259	0.03

Note: Note: Coordinates are based on the Montreal Neurological Institute coordinate system. Regions are based on the Harvard-Oxford Cortical Structural Atlas.

Table 3.3

Regions with functional connectivity to inhibitory control FPCN mask predictive of memory scores.

Contrast	Cluster location	Regions	Peak	Size	p-value
Self Up	Bilateral striatum	Left Prefrontal Thalamus Right Prefrontal Thalamus Left Putamen Right Putamen Left Caudate Right Caudate Left Accumbens	-8, -24, 8	1852	2.8E-06
Self Up, LG Down	Left striatum	Left Thalamus Left Putamen Left Accumbens	-8, -24, 8	797	0.0024

Note: Coordinates are based on the Montreal Neurological Institute coordinate system. Regions are based on the Harvard-Oxford Subcortical Structural Atlas and on the Oxford Thalamic Connectivity Probability Atlas. LG = Lady Gaga

Table 3.4

Regions with functional connectivity to self-referential DMN mask predictive of inhibitory control

Contrast	Cluster location	Regions	Peak	Size	p-value
Good inhibitory control	Right OFC	Frontal operculum cortex Inferior frontal gyrus pars triangularis pars opercularis Frontal orbital cortex Insular cortex	40, 24, -4	430	0.02

Note: Coordinates are based on the Montreal Neurological Institute coordinate system. Regions are based on the Harvard-Oxford Cortical Structural Atlas, OFC: Orbitofrontal Cortex

3.5 Discussion

The current study found that as efficiency scores at inhibitory control got better the magnitude of the self-reference effect decreased. In particular, better inhibitory control scores were related to reduced memory for self-related material when this was accompanied by good memory scores on the non-self control condition, in comparison to inhibitory control when memory scores were high in both self and non-self conditions. This finding allows us to rule out the possibility that the reduced self-reference effect linked to inhibitory control was being driven by higher Lady Gaga scores, as this effect was still found within individuals with equally high memory for Lady Gaga. Following the assumption that a higher self-reference effect is indicative of an increased tendency for self-focussed attention, confirmed by the relationship found between the magnitude of the self-reference effect and inhibitory control efficiency, these results support our postulated theory that a salient self can act as a powerful distractor.

Exploration of the neural resting-state correlates of this inhibitory control-self-reference relationship revealed that the functional connectivity of the FPCN regions identified during No-Go trials predicted the magnitude of the self-reference effect. In particular individuals with a reduced self-reference effect, i.e. those with the best inhibitory control, had stronger functional connectivity between inhibitory control regions and a subcortical cluster located in the ventral regions of the left caudate and putamen, as well as in the dorsomedial nucleus of the thalamus that projects to the prefrontal cortex (Groenewegen 1988; Ray & Price 1993). Meta-analytic decoding of

the functional connectivity of this subcortical cluster using Neurosynth related this cluster to terms such as “reward” and “anticipation”. Extensive research has found the ventral striatum to be involved not only in reward processing but also in assigning self-specificity to stimuli (for a review see Northoff & Hayes, 2011), aiding our interpretation of why the functional connectivity of this subcortical cluster was predictive of the magnitude of the self-reference effect. In particular, stronger functional connectivity between the striatum and the FPCN was related to a reduced self-reference effect. Shedding light on why a stronger, and not a weaker, functional connectivity between reward and control systems lead to a reduced self-reference effect, Dong, Lin, Hu, Xie and Du (2015) have shown that the functional connectivity between the nucleus accumbens and the executive control network is inversely related to the functional connectivity between the accumbens and the reward system and that this relationship is disturbed in compulsive internet gamers. This lead the authors to conclude that these two systems (i.e., control and reward) act in a “pull and push fashion”, in such a way that the inhibition of motivational desires coded in the reward system is executed through strong control signals originated in the FPCN. On the other hand, heightened motivational signals will instead lead to a failure of executive control over immediate rewards. Our current study found an enhanced functional connectivity between FPCN and the left accumbens linked to a reduced self-reference effect. Hence, based on Dong’s research (2015) it is possible that this pattern of functional connectivity between FPCN and ventral striatum reflects an enhanced control over automated behaviour linked to mind-wandering about self-relevant material. In support of this, neuropsychological research has found that patients with damage to regions in the FPCN show a hyper self-bias (Sui, Enock, Ralph & Humphreys, 2015), suggesting an inability of these patients to suppress salient self-related material. Hence, the enhanced functional connectivity between FPCN and reward systems, closely related to self-related processing (de Greck et al., 2008; Enzi, De Greck, Proesch, Tempelmann & Northoff, 2009; Ersner-Hershfield, Garton, Ballard, Samanez-Larkin & Knutson, 2009), might be reflecting one’s ability to suppress meaningful internal representations when the context requires it. In turn, it is plausible that this heightened suppression over self-related processing is manifested as the reduced self-reference effect linked to this pattern of functional connectivity.

In support of this suppressive role of the striatum, extensive research has shown that the striatum is a main component of the circuits involved in suppression and initiation of movement. For example, activity in striatum has been previously related to successful suppression of responses during stop-signal response paradigms (Aron & Poldrack 2006). Despite these structures have predominantly been studied in relation to initiation and suppression of movement, recent research has revealed these regions to also be recruited when thoughts need to be suppressed. In particular, a meta-analysis performed by Guo, Schmitz, Mur, Ferreira and Anderson (2018) found similar activations in the basal ganglia during a think/no think paradigm and a stop signal response task, suggesting a domain-general role of the basal ganglia for action and memory cancellation. Assuming the reduced self-reference effect linked to the FPCN-striatum pattern of functional connectivity emerges from a stronger tendency to suppress DMN-related material, our results suggest that this pattern of functional connectivity might be allowing the suppression of intrusive self-focussed attention, manifested as a reduced self-reference effect in the current study.

Our other resting-state analysis using as seed region DMN regions identified during self-referential processing, revealed a pattern of functional connectivity predictive of GNG efficiency. In particular, stronger functional connectivity to a cluster in the right orbitofrontal cortex extending into the right insula predicted better inhibitory control. The functional connectivity of this cluster was related to terms like “response inhibition” and “stop signal”. Extensive research has found the lateral orbitofrontal cortex, and in particular the pars opercularis to be related to inhibitory control. For example, Chambers and colleagues (2006) disrupted inhibitory control by applying transcranial magnetic stimulation to this area. In addition, performance at stop-signal paradigms is also disrupted by lesions to this region (Aron, Fletcher, Bullmore, Sahakian & Robbins, 2003). In addition, a meta-analysis of OCD patients (Rotge et al., 2010), characterised by an inability to suppress self-referential thinking, uncovered a cluster located in the lateral orbitofrontal cortex that closely overlaps with the right orbitofrontal cluster found in the current study. Hence, it is possible that stronger functional connectivity between right orbitofrontal cortex and areas involved

in self-reference is linked to better inhibitory control through allowing suppression of self-referential cognition.

In order to explore functional commonalities between the two clusters found in the current study (i.e., the subcortical cluster related to reward and the orbitofrontal cluster related to inhibitory control) a conjunction analysis of the group maps obtained for each cluster was performed. This conjunction analysis revealed a map that overlapped mostly with the salience network as defined by Yeo et al (2011). There was also a strong overlap with regions of the DMN, and on a lesser extent, with the limbic and FPCN networks. Using a subcortical parcellation of resting-state networks within the basal ganglia (Choi, Yeo & Buckner, 2012) we found that our conjunction map overlapped most strongly with regions of the basal ganglia functionally connected primarily to the FPCN but also to the DMN and the salience network. Taking into consideration the conjunction analysis our results point towards patterns of functional connectivity that connect the executive, salience and default mode networks through the striatum, in a manner that controls the balance between self-reference and inhibitory control.

In addition to being related to self-specificity (Northoff & Hayes, 2011), the reward processing centres anchored in the striatum are part of the salience network (Seeley et al., 2007). These three concepts, (i.e., self-specificity, reward and salience) are closely associated: stimuli that are relevant to the self (self-specificity) are those to which the self has assigned value to (reward) and hence will have a strong tendency to attract attentional resources (salience) anchored in the FPCN. Several studies have suggested that the salience network, and in particular the insular cortex, plays an important role in coordinating the DMN and the FPCN networks. Sridharan, Levitin and Menon (2008) have shown that the right fronto-insular cortex, in close proximity with the cluster found in the current study and a main hub of the salience network, plays a casual role in activating the FPCN and deactivating the DMN during tasks that required external attention. Our analyses revealed that stronger functional connectivity between the right orbitofrontal cortex, strongly coupled to the salience network, and the DMN resulted in better inhibitory control, suggesting this DMN-orbitofrontal cortex pattern of functional connectivity, through its coupling to the

salience network, might play a pivotal role in suppressing internally generated representations. In addition, Seeley and colleagues (2007) argue that, based on subjective salience, the salience network signals to the FPCN what information to operate on. It is therefore possible that instances of poor performance during sustained attentional tasks are due to internal representations processed in the DMN being signalled as more salient than external stimuli, attracting attentional resources away from the task. If this was the case, increasing the salience of task-stimuli through incentivising should improve task performance, as has repeatedly been observed in the literature (Jenkins, 1998; Leon & Shadlen, 1999).

It is therefore possible that the psychological underpinning of failure at sustained attention, manifested as poor inhibitory control, relates to an excessive salience of self-related material that fixates attentional resources away from the task-related material. If this self-related material acts as a powerful distractor, then individuals with a higher self-bias should have worse performance at inhibitory control tasks as we have observed in the current study. The current study cannot however rule out the opposite possibility, i.e., that the reduced inhibitory control linked to the self-reference effect does not originate from an excessive salient self but that instead the increased self-reference effect is the result of impaired inhibitory control. Whether a heightened self leads to worse inhibitory control or whether worse inhibitory control leads to a heightened self will have to be specifically addressed in future studies. Both options are not mutually exclusive, however, based on the known distracting effect of emotions (Dolcos & McCarthy 2006; Mueller, 2011) and on the inherent salience of self-relevant material due to its high assigned value, it is tempting to speculate that the former option is more self-explanatory. In contrast, the latter option, i.e., bad inhibitory control leads to increased self-reference effect, would still leave unanswered why the inhibitory control is impaired in the first place. This effect was found in patients with damage to the FPCN however, considering the subjects used in the current study were healthy individuals, this option seems unlikely.

Despite an inflexible tendency to direct attention towards the self is characteristic of many psychopathological conditions such as depression and anxiety (for a review see Ingram, 1990), which have extensively been related to impaired

executive function (Ansari & Derakshan, 2011; Kaiser et al., 2003), to our knowledge this is the first study that directly relates both of these measures, revealing a relationship within healthy subjects. The behavioural correlation found between the magnitude of the self-reference effect and inhibitory control, in combination with the cross-sectional design used in the resting-state analyses suggests that the magnitude of the SRE can be used as an objective measure of self-focussed attention and that self-related material can act as a powerful distractor. In turn, the ability to suppress such material appears to be related to patterns of functional connectivity that couple the DMN, salience and FPCN networks through mechanisms that are anchored in the basal ganglia.

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Chapter 4: That's me in the Spotlight: Neural Basis of Individual Differences in Self-Consciousness

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4.1 Abstract

A long-standing literature implicates activity within the DMN to processes linked to the self. However, contemporary work suggests that other large-scale networks might also be involved. For instance, goal-directed autobiographical planning requires positive functional connectivity between DMN and FPCN networks. The present study examined the inter-relationship between trait self-focus (measured via a self-consciousness scale; SCS), incidental memory in a self-reference paradigm, and resting-state functional connectivity (FC) of large-scale networks. Behaviourally, we found that private SCS was linked to stronger incidental memory for self-relevant information. We also examined how patterns of FC differed according to levels of self-consciousness by using the SCS data to drive multiple regression analyses with seeds from the DMN, the FPCN and the limbic network. High levels of SCS was not linked to differences in the FC of the DMN, however, it was linked to stronger coupling between FPCN and a cluster extending into the hippocampus, which meta analytic decoding using Neurosynth linked to episodic memory retrieval. Subsequent analysis demonstrated that trait variance in this pattern of FC was a moderator for the observed relationship between private SCS and enhanced memory for self-items. Together these findings suggest that interactions between the FPCN and hippocampus may support the memory advantage of self-relevant information associated with SCS and confirm theoretical positions that argue that self-related processing does not simply depend upon the DMN, but instead relies on complex patterns of interactions between multiple large-scale networks.

4.2 Introduction

Human cognition is characterised by the capacity for self-consciousness – the process through which we can become the subject of our own conscious experience. The degree to which individuals engage in self-consciousness appears early in development (Berthenthal & Fischer, 1978; Lewis & Brooks, 1978; Lipka & Brinthaupt, 1992), and it can have both positive and negative outcomes in daily life. For example, the ability to reflect on our own thoughts and actions is crucial for the development of personal identity (Turner, 1978); however, when taken to extremes, the same process can result in excessive shyness or anxiety (Crozier, 2002). A well established measure of self-consciousness (Carver & Glass, 1976; Scheier & Carver, 1985; Scheier & Carver, 2013) divides the construct into three related, yet independent, dimensions: 1) private self-consciousness, which describes the extent to which people introspect and examine hidden aspects of the self (e.g., their beliefs or values), 2) public self-consciousness, which describes the extent to which people examine how public aspects of the self may be perceived by others (e.g., what impression others might form), and 3) social anxiety, which describes the extent to which people react to perceptions of their public self and evaluations from others.

When people engage in self-conscious thought, schema containing self-relevant information are activated (Nasby, 1985) and this information possesses special mnemonic qualities. For example, people have a robust tendency to remember information more effectively when it is processed with respect to the self, a bias resulting in better memory recall for self-related information (termed “The self-reference effect”; Rogers et al, 1977). One possibility is that the self-reference effect is simply an indirect consequence of familiarity: self-relevant information is likely to be highly familiar and familiarity is known to facilitate encoding (Prentice, 1990). However, research has ruled out familiarity as the mechanism underlying the self-reference effect because a self-referent bias has also been observed for neutral shapes (Humphreys & Sui, 2015) and everyday items (Cunningham et al., 2011). Instead, self-reference is thought to improve memory because of the rich network of associations associated with ourselves which in turn allows for the formation of stronger memory traces (Symons & Johnson, 1997). As well as its effect on memory,

self-relevant information has strong salient properties which impact on attention (Sui et al, 2015), with studies showing that one's name (Harris & Pashler, 2004) or face (Bredart et al, 2006) can act like an efficient distractor. Moreover, other studies have shown that self-relevant information has similar properties to salient perceptual stimuli, automatically triggering the reallocation of attentional resources (Sui et al, 2015). These experimental paradigms share similarities with more naturalistic mental processes such as mind-wandering, where salient self-relevant information becomes the focus of conscious attention when we are otherwise engaged in external tasks (Smallwood et al., 2011). Although mind-wandering can often be associated with task errors (McVay & Kane, 2009; Weissman et al., 2006), the reallocation of attention towards the self during a task may serve a broader function because it can facilitate the processing of personally meaningful goals that extend beyond the here-and-now (Medea et al., 2016; for a review see Poerio & Smallwood, 2016).

Recent neuro-imaging work has examined the neural basis of the process of self-reflection, a process important for self-consciousness (Grant et al., 2002). Task-based studies of self-reference often observe activity in the mPFC, as well as regions in the posterior cingulate cortex (Kelley et al., 2002, Macrae et al., 2004; Northoff et al., 2006), regions that collectively form what is known as the default mode network (DMN). This large-scale network tends to show a pattern of deactivation during demanding external tasks (Raichle et al, 2001) and shows coherent activity during the resting-state (Greicius et al., 2003). In addition, the DMN has also been linked to states of self-generated thought, such as mind-wandering (for recent meta-analyses see Fox et al., 2015; Stawarczyk & D'Argembeau, 2015). Recent work, however, suggests that the DMN often works in tandem with the other networks when internal representation must be manipulated in a goal directed fashion. For example, regions of lateral frontal and parietal cortex (that together form the FPCN), become coupled with the DMN when autobiographical information is organised to form a plan (Spreng et al., 2010) and when identifying perceptual aspects of semantic processing (Krieger-Redwood et al., 2016). Moreover, extensive research has related regions in the FPCN to sustained attention and working memory (Coull et al., 1996, Koechlin et al., 1999; Rottschy et al., 2012), processes that allow conscious manipulation of information. These findings, along with those from Spreng and colleagues (2010), suggest that

processing of self-related information present during self-consciousness may recruit the executive system anchored in the FPCN. It is a possibility that differences across individuals in their attentional preferences, i.e., how often one engages in self-conscious thought versus other types of information, is reflected in the functional connectivity of the FPCN.

Moreover, a study conducted by Eisenberger and colleagues (2005) found a relationship between activity in a cluster in the FPCN, namely in the dorsal anterior cingulate cortex, and self-consciousness during a vigilance task. Similarly, studies have shown that when participants hold social information in mind they use lateral regions of cortex linked to executive control processes (Meyer et al., 2012). In addition to the DMN and the FPCN, the limbic system may also play an important role in self-oriented cognition. Extensive research has shown that negative mood increases self-focused attention (Sedikides, 1992) as well as mind-wandering (Poerio et al., 2013; Smallwood et al., 2009) and some studies have suggested that the effect of mood on information processing in turn predicts later behaviour (Gendolla, 2000). Moreover, neuroimaging research has shown a distinction within the mPFC between cognitive and affective components of self-oriented cognition (Moran et al., 2006) while the amygdala, a main hub of the limbic system, is important in a range of psychiatric conditions associated with disturbances in the self (Davidson 2002; Phan et al., 2006; Strakowski et al., 1999).

The current study aimed to determine the functional architecture that underpins different forms of self-consciousness (private, public and social anxiety) and to understand how this is related to the strength of a person's memory for self-relevant information. We recorded functional imaging data in a large cohort of participants during wakeful rest who later completed the three subscales of the Self-Consciousness Scale (Scheier & Carver, 2013). Previous research has consistently found a positive relationship between private self-consciousness scores and the magnitude of the self-reference effect (Agatstein & Buchanan, 1984; Hull et al., 1988; Nasby, 1985; Turner, 1980) and so in this experiment we also measured incidental memory for self-relevant information in our participants. We hypothesised that differences in response on the self-consciousness scale should be reflected in the connectivity patterns of three large-scale networks (Default Mode, Frontoparietal

Control and Limbic). To select these large-scale networks we used a parcellation obtained by Yeo and colleagues who applied clustering techniques to resting-state data of 1000 individuals (Yeo et al., 2011).

We were interested in (a) replicating prior findings linking high levels of private self-consciousness to better memory for the self, (b) identifying patterns of functional connectivity of the DMN, FPCN and Limbic networks associated with different aspects of self-consciousness and (c) determining whether any neurocognitive patterns linked to different types of self-consciousness explained the hypothesised self-memory advantage.

4.3 Methods

4.3.1 Participants

A hundred and forty one healthy right-handed participants were recruited to the study; in exchange for participation they received a monetary reward or course credits. The sample had an average age of 22.50 (SD = 2.93) years. Approval for this project was granted by the York Neuroimaging Centre (YNiC) Ethics Committee and was conducted in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.

4.3.2 Procedure

4.3.2.1 Self- Consciousness Scale

Participants completed a 22-item version of the self-consciousness scale inventory (Scheier & Carver, 2013) from which three subscales can be derived: private self-consciousness, public self-consciousness and social anxiety. Private self-consciousness is a measure of the tendency that an individual has to introspect and study one's inner self and motives and was assessed with nine statements such as "I'm always trying to figure myself out". Public self-consciousness refers to the tendency of an individual to think about what others think about him/her, and was assessed through seven statements such as "I care a lot about how I present myself to others" Finally social

anxiety was measured with six statements such as “It takes me time to get over my shyness in new situations”. Participants had to answer to each statement using a scale from 0 (not at all like me) to 3 (a lot like me). Items from each subscale were summed to create an overall score per scale.

4.3.2.2. Self-Reference Paradigm

This paradigm asked individuals to process words in either 1) relation to themselves, 2) relation to an unfamiliar other (Lady Gaga) or 3) relation to the number of syllables. This judging phase was followed by a surprise retrieval phase in which participants were presented with a word and had to decide whether that word had been presented during the judging phase or whether it was a new word. A source localisation question followed all the words judged as old and memory scores were calculated for each condition. For more details of how the task was ran see Chapter 3.

4.3.3 Resting-state

4.3.3.1 Scan Acquisition

Functional MRI data was acquired on a 3 Tesla GE scanner. Participants observed a fixation cross for a scan that lasted 9 minutes. The scan had a repetition time of 2 seconds, resulting in 210 volumes. We used interleaved slice-timing and isotropic voxel dimensions of 3 mm³ (matrix size of 64 X 64, 192mm field of view, and 32 slices) with a 0.5mm gap between slices.

4.3.3.2. Pre-processing

All fMRI preprocessing and analysis was performed using FSL. We extracted the brain from the skull using the BET toolbox for both the flair and the structural T1 weighted images and these scans were registered to standard MNI152 (2mm) space using FLIRT (Jenkinson & Smith, 2001). Prior to conducting the functional connectivity analysis, the following prestatistics processing was applied to the resting-state data; motion correction using MCFLIRT (Jenkinson et al., 2002); slice-timing correction using Fourier-space time-series phaseshifting; non-brain removal using BET (Smith 2002);

spatial smoothing using a Gaussian kernel of FWHM 6mm; grand-mean intensity normalisation of the entire 4D dataset by a single multiplicative factor; highpass temporal filtering (Gaussian-weighted least-squares straight line fitting, with sigma = 100 s; Gaussian lowpass temporal filtering, with sigma = 2.8s.).

4.3.3.3. First Level Analysis

Following these steps, the time series of 3 masks of interest were extracted. These masks corresponded to 1) the DMN, 2) the FPCN and 3) the limbic system as defined by the 7 network parcellation performed by Yeo and colleagues (Yeo et al., 2011) and can be visualised in Figure 4.2. The approach of selecting large-scale network masks was based on previous studies using dual-regression, in which networks obtained through ICA group analyses are used as regions of interest in subsequent seed based analyses (Zuo et al., 2010; Rytty et al., 2013; Smith et al., 2014). Instead of using ICA group masks as regions of interest the current study used a reliable parcellation based on 1000 subjects (Yeo et al., 2011).

The parcellations in non-linear MNI152 volume space were downloaded from https://surfer.nmr.mgh.harvard.edu/fswiki/CorticalParcellation_Yeo2011 and resampled from 1mm³ to 2mm³. The time series for each voxel within each mask were averaged and used as an explanatory variable in a subject-level functional connectivity analysis, which also included the following nuisance regressors: the first five principal time-series components extracted from white matter (WM) and cerebrospinal fluid (CSF) masks in accordance with the CompCor method (Behzadi et al. 2007) and six motion parameters. WM and CSF masks were generated by segmenting each individual's high-resolution structural image (using FAST in FSL). The default tissue probability maps, referred to as Prior Probability Maps (PPM), were registered to each individual's high-resolution structural image (T1 space) and the overlap between these PPM and the corresponding CSF and WM maps was identified. Finally, these maps were thresholded (40% for the SCF and 66% for the WM), binarised and combined. The six motion parameters were calculated in the motion-correction step during pre-processing. Linear displacements in each of the three Cartesian

directions (x, y, z) and rotations around three axes (pitch, yaw, roll) were included for each individual. No global signal regression was performed (Murphy et al., 2009).

4.3.3.4. Second Level Analysis.

To understand whether our psychological measures of self-consciousness varied with either the between or within connectivity of the DMN, limbic and the FPCN, we used FSL to conduct a group-level regression of the connectivity matrices of each mask. In this analysis we included the residualised mean centred scores for the three self-consciousness subscales as regressors of interest. In order to control for spurious correlations related to subject motion we included framewise displacement as a regressor of no interest, after controlling for four outliers by imputing their data to 2 standard deviations (Power et al., 2012). See Sormaz et al., (2017) for a prior demonstration of this approach. This technique allows us to examine regions within or outside the network mask whose connectivity varies with particular traits (in this case different aspects of self-consciousness). In these analyses the data were processed using FEAT version 5.98 part of FSL (FMRIB's Software Library, www.fmrib.ox.ac.uk/fsl) and the analyses were carried out using FMRIB's Local Analysis of Mixed Effects (FLAME). A grey matter mask with a probability threshold of 40% was used as a pre-thresholding mask and the cluster-forming threshold was set as z-score of 2.3. For these analyses we controlled for Type I errors by controlling for the number of voxels in the brain (Worsley 2001), as well as the number of masks and the two tailed nature of our comparisons yielding an alpha value of $p < .008$ FWE.

4.3.4 Neurosynth Meta-Analyses

In order to interpret neuro-cognitive patterns of functional connectivity predictive of self-consciousness, we performed a meta-analysis using the online Neurosynth database (Yarkoni et al., 2011). We performed a meta-analytic decoding of the unthresholded maps produced in this study by uploading them onto Neurosynth. This allows the identification of psychological terms that are most likely to be associated with the specific spatial pattern that our analysis highlighted providing a quantitative interpretation of our data (for a prior illustration of this technique see de Sormaz et

al., 2017). For the purposes of interpretation we selected the 15 terms most related to the current spatial maps and displayed them in the form of word clouds in which a larger font size indicated a greater probability of association.

4.4 Results

4.4.1 Behavioural

4.4.1.1. Self-consciousness scale

The three subscales (private, public and social anxiety) for the self-consciousness questionnaire were calculated for each individual. The public subscale was correlated with both the private ($r = .40, p < .001$) and the social anxiety scale ($r = 0.35, p < .001$). No significant correlations were found between the private and the social anxiety subscales ($r = .11, p = .235$). In order to control for these correlations, the standardised residual scores were used in further analyses.

4.4.1.2. Self-Reference Paradigm

The first aim of our study was to establish whether in our sample we found a reliable self-relevant memory advantage. A repeated measures one-way analysis of variance (ANOVA) using the proportion of hits for each referent as the within-participants factor indicated a significant effect of referent on incidental memory performance ($F(2, 278) = 284, p < .001, \eta^2 = .672$), as measured during the retrieval phase of the self-other reference paradigm. Post-hoc paired-samples *t*-tests were conducted to compare incidental memory across the three conditions (self, Lady Gaga, syllable count). Participants had significantly better memory in the self ($M = 0.78, SD = 0.15$) compared to the Lady Gaga ($M = 0.62, SD = 0.19$) condition; $t(139) = 10.85, p < .001, d = .92$; they also showed significantly better memory in the self condition compared to the syllable count ($M = 0.4, SD = 0.18$) condition; $t(139) = 23.56, p < .001, d = 1.99$. Participants also had significantly better memory in the Lady Gaga compared to the syllable condition; $t(139) = 12.87, p < .001, d = 1.09$ (Figure 4.1A). In addition, examination of the confidence intervals obtained from one-sample *t*-tests suggested memory for the syllable condition was at chance (95% CI [.37,.44]), whereas memory

for Lady Gaga (95% CI [.60,.66]) and self (95% CI [.76,.81]) were both above chance performance.

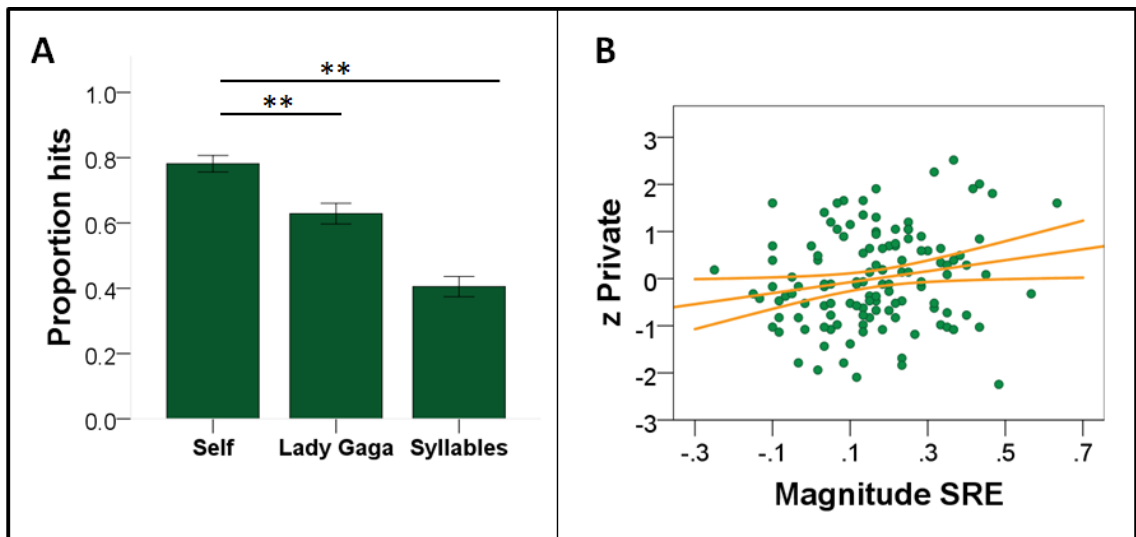


Figure 4.1: A) ANOVA results between memory scores for the 3 conditions. B) Scatterplot reflecting correlation between the standardised residual score for private self-consciousness and the magnitude of the self-reference effect (SRE).

4.4.1.3. Private Self-Consciousness and Magnitude of the Self-Reference Effect

Next, we sought to identify whether in our sample individuals high in private self-consciousness have a stronger memory when referring information to themselves rather than a familiar other (Agatstein & Buchanan, 1984; Hull et al., 1988; Nasby, 1985; Turner, 1980). In order to explore this possibility, we conducted a repeated measures analysis of covariance (ANCOVA). The within-subject factors included the main effects for the incidental memory for self and Lady Gaga items (corrected for guessing). The different types of self-consciousness scores were included as between participant covariates. This analysis revealed a significant interaction between the incidental memory for the two referents and the private self-consciousness scale ($F(1,116) = 5.041, p < .05$). Post hoc analyses demonstrated a significant positive correlation between the magnitude of the self-reference effect and private self-consciousness ($r = .19, p < .035$) (Figure 4.1B). Based on previous research revealing that familiarity has a significant influence on memory, familiarity ratings for Lady Gaga

were obtained at the end of the experiment. A partial correlation controlling for the Lady Gaga familiarity ratings still showed a positive and significant correlation between the private self-consciousness scores and the magnitude of the self-reference effect both controlling for false alarms ($r = .18, p = .030$) and without controlling for false alarms ($r = .19, p = .035$). Together these analyses allowed us to establish in our sample that private self-consciousness is linked to a stronger memory for information referred to the self.

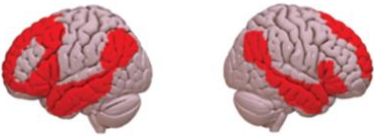
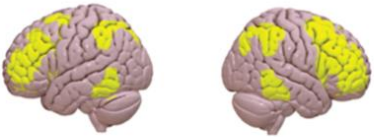

Masks taken from Yeo networks	
DMN	
FPCN	
Limbic	

Figure 4.2: Masks taken from Yeo et al (2011) parcellation. Top row: Default-mode network (DMN). Middle row: Frontoparietal Control Network (FPCN). Bottom row: Limbic network

4.4.2 Resting-state fMRI

Next, we explored whether self-consciousness is reflected in the brain's intrinsic connectivity by performing a seed based analyses on the DMN, FPCN and limbic networks defined by the 7 network parcellation from Yeo and colleagues (Yeo et al., 2011). We calculated the correlation between the time series for each of these

networks and each voxel in the rest of the brain for each individual. The functional connectivity group maps obtained for each network can be visualised in Figure 4.3. Next, we used these spatial maps as the dependent variable in a series of multiple regressions using the standardised residuals of each component of the self-consciousness scale as explanatory variables. Correction for multiple comparisons included a whole brain correction, correction for two-tailed tests and correction for the number of seeded locations (3), yielding an alpha value of $p = .008$ FWE.

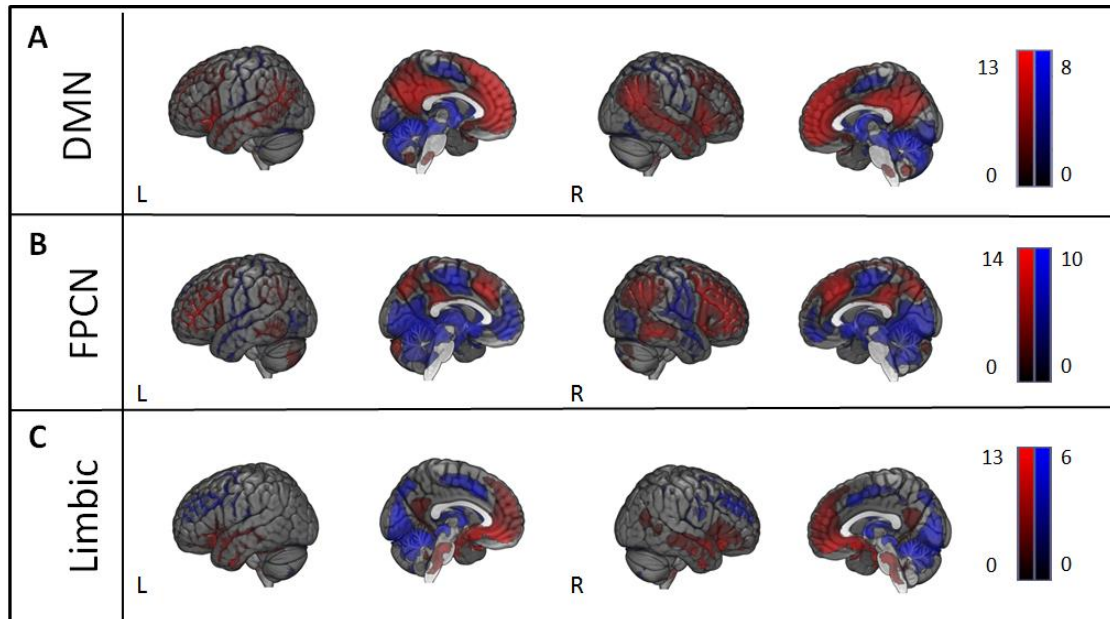


Figure 4.3: *Functional connectivity (FC) group maps.* A) Default Mode network (DMN) B) Frontoparietal Control Network (FPCN). C) Limbic Network. Red and blue colours represent positive and negative functional connectivity, respectively.

We found two patterns of functional connectivity that varied with different types of self-consciousness. The FPCN revealed a pattern of stronger functional connectivity between this network and a cluster with a peak in the temporal occipital fusiform cortex that extended into the hippocampus with greater levels of private self-consciousness (Figure 4.4, top row). The unthresholded map for this contrast can be found at Neurovault at the following link: <http://neurovault.org/images/39599/>. Possibly due to the fusiform nature of the cluster, metaanalytic decoding using Neurosynth revealed terms such as “objects”, however it also revealed terms such as “episodic”, “recognition” and “episodic memory” terms which are consistent with the hypothesised relationship between mnemonic processes and high levels of private self-consciousness. The limbic network revealed a pattern of functional connectivity to the occipital cortex predictive of social anxiety. In particular, stronger functional connectivity between these regions was predictive of higher social anxiety scores (Figure 4.4, bottom row). The unthresholded map for this contrast can be found at this link: <http://neurovault.org/images/39600/> and meta-analytic decoding revealed this map to be related, among others, to the term “face”, which is in line with the social nature of this type of anxiety. Finally, analyses of the DMN did not reveal any patterns of functional connectivity predictive of either types of self-consciousness that passed

correction for multiple comparisons, although all unthresholded maps are available at the following URL:<http://neurovault.org/images/43237/> and <http://neurovault.org/collections/2284/>. To understand these patterns of data in greater detail we extracted the connectivity with the relevant networks and the region identified through our analyses and plotted these as scatterplots in each figure. The details of these clusters can be found in Table 1.

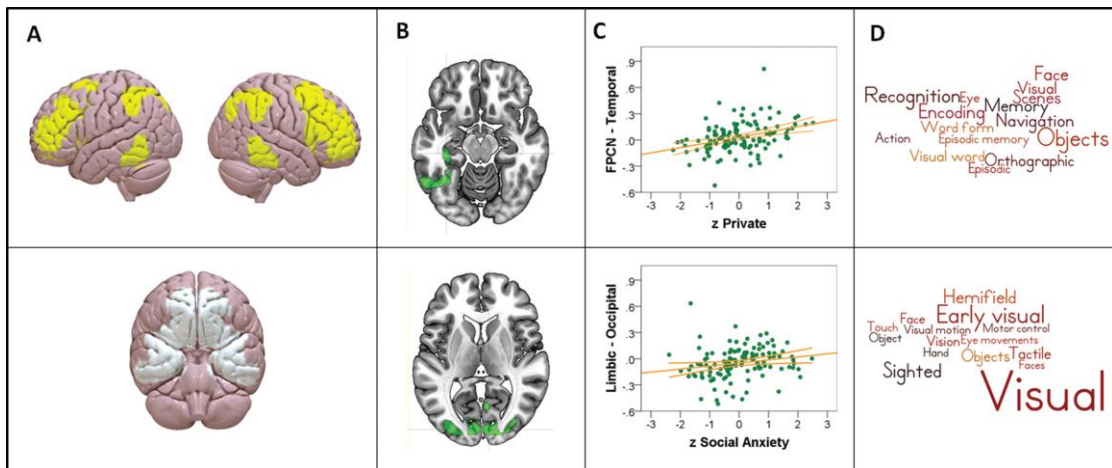


Figure 4.4 Association between seed regions and clusters predictive of self-consciousness. Top row: results for the Frontoparietal Control Network. Bottom row: Results for the Limbic Network. A) Seed region. B) Cluster with functional connectivity (FC) predictive of self-consciousness. C) Scatterplot reflecting relationship between FC and self-consciousness. D) Neurosynth’s meta-analytic decoding of cluster in B.

4.4.3 Moderation Analysis

Having identified that private self-consciousness is linked to better memory for information related to the self and that it is also associated with patterns of functional organisation at rest, we next explored whether the expression of better self memory can be related to these patterns of functional organisation. In these analyses we used the correlation coefficients between the FPCN and the cluster in the temporal occipital fusiform cortex as a moderator of the relationship between private self-consciousness and the task outcomes. Moderation analyses using PROCESS (Hayes, 2013) revealed that the functional connectivity between the FPCN and the temporal occipital fusiform cluster moderated the relationship between private self-consciousness and the magnitude of the self-reference effect, $\Delta R^2 = .037$, $F(1, 119) = 4.846.08$, $p < .05$. This can be visualised in Figure 4.5 in which the data has been divided using a median split

of the functional connectivity coefficients. Here it is apparent that the positive relationship found between private self-consciousness and the magnitude of the self-reference effect is present in individuals with a high functional connectivity between the FPCN and the temporal occipital fusiform cortex ($r = .334, p = .011$) and absent in individuals situated below the median ($r = .03, p = .812$) (Figure 4.5B).

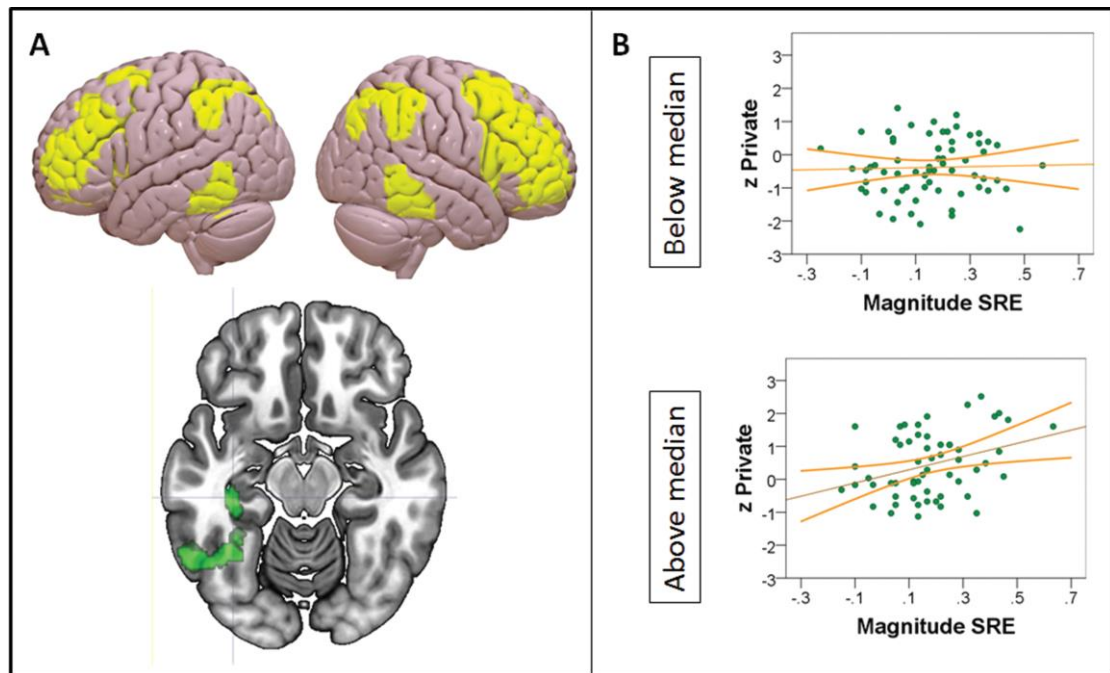


Figure 4.5: Moderation of the relationship between memory for self-items and private self-consciousness by the functional connectivity of the Frontoparietal Control Network (FPCN). A) FPCN (yellow) and cluster with functional connectivity (FC) to the network predictive of private self-consciousness (green). B) Median split of FC between FPCN and cluster. Top: Scatterplot reflecting the lack of relationship between memory for self-items and private self-consciousness in the below median group. Bottom: Scatterplot reflecting the positive correlation between memory for self-items and private self-consciousness in the above median group

Table 4.1

Regions that exhibit functional connectivity to seed dependent upon self-consciousness scores

Seed	Contrast	Cluster	Regions	Peak	#voxels	p-value
FPCN	Private Up	Temporal	post inferior temp temp occip fusiform parahippocampal hippocampus	-48,-52,-28	1085	.006
Limbic	Social Anxiety Up	Occipital	inf lat occipital intracalcarine lingual gyrus	-8,-90,10	1324	.001

Note: Coordinates are based on the Montreal Neurological Institute coordinate system and regions are based on Harvard-Oxford Cortical Structural Atlas.

Abbreviations: post: occip: occipital; posterior; temp: temporal

4.5. Discussion

Our data suggest that the tendency towards private self-consciousness is characterised by a memory bias for self-relevant information that is rooted in the functional organisation of the brain at rest. We replicated prior studies showing that high levels of private self-consciousness are associated with a mnemonic advantage for self-relevant information (Agatstein & Buchanan, 1984; Hull et al., 1988; Nasby, 1985; Turner, 1980). Our functional connectivity analyses indicated that private self-consciousness was also associated with strong connectivity between the FPCN and regions of lateral occipital cortex, fusiform cortex and hippocampus, a pattern that meta-analytic decoding suggests is often associated with functions including episodic memory. Critically, our moderation analysis demonstrated that these two effects are related: we found that the relationship between private self-consciousness and a heightened memory for the self was only present in participants who exhibited this episodic neural fingerprint at rest. Taken together, our results suggest that patterns of neural organisation associated with the effective retrieval of episodic details may be central to the ability to consciously reflect on who we are as indexed by private self-consciousness.

They also support functional studies linking executive regions to process of self-consciousness (Eisenberger et al., 2005) and when working memory is focused on more personally relevant information (Meyer et al., 2012). Our study also raises the question of whether these patterns exhibited by individuals high on private self-consciousness may also have a relationship to the thoughts experienced during the resting-state, a question that could be addressed using experience sampling after resting-state scans (for examples see Gorgolewski et al., 2014, Smallwood et al., 2016). Unlike private self-consciousness, we found that social anxiety was related to heightened connectivity between the limbic network and regions of visual cortex. It is not surprising that the functional connectivity of the limbic system predicted social anxiety scores, given the well documented links between these regions and emotion (Cardinal et al., 2002; Davidson 2002; Phan et al., 2006; Phelps & DeLoux, 2005; Strakowski et al., 1999).

Moreover, our analysis suggests that social anxiety is linked to heightened connectivity between the limbic system and regions of occipital cortex, a pattern that may explain the hyper vigilance to social cues that are often associated with this form of self-consciousness (Eysenck 1992; Mogg & Bradley 1998). Thus unlike private self-consciousness, which was linked to heightened memory, our data is consistent with the view that social anxiety is linked to an attentional bias concerned with external attention, potentially to the reaction of other people to the public self (Bogels & Mansell, 2004; Mueller et al., 2009). It will be important in the future to determine whether the pattern of functional connectivity that we show supports social anxiety is a moderator for some of the attentional biases that this trait has been linked to in the past.

Our analysis did not link the DMN to any of the types of self-consciousness measured in our study. Our analytic strategy highlights differences between types of self-consciousness, so it is possible that the absence of any observed associations with the DMN may be because this network plays a role common to all three types of self-consciousness. Given evidence that the DMN is activated by states of self-focus (Andrews-Hanna et al., 2014; Northoff et al., 2006) perhaps the absence of an association with this system reflects the fact that it is generally important in all states of self-consciousness, rather than in the expression of specific types. On the other hand, our observation that private self-consciousness is described by the connectivity of the FPCN supports accounts of states of self-focus which have linked self-biases to the function of regions of the control networks such as the interparietal sulcus (Sui et al, 2015; Humphreys & Sui 2016). More broadly, our findings are consistent with theoretical positions that advocate a more complex component process architecture for states of higher-order cognition, such that different types of cognition emerge through the interaction of multiple different large scale networks (for examples see Ralph et al., 2016; Moscovitch et al., 2016; Smallwood and Schooler, 2015). For example, an emerging literature has begun to show that the DMN is important in many situations beyond those linked to internal focus, such as working memory (Konishi et al., 2015; Vatansever et al., 2015), social memory (Meyer et al., 2012), or demanding semantic task performance (Krieger-Redwood et al., 2016), observations that are consistent with the notion that the DMN acts to integrate information from across the

cortex (Margulies et al., 2016). For example, research exploring autobiographical planning has shown co-activation in the FPCN and medial temporal lobe structures (e.g., the hippocampus) when we consider future goals (Gerlach et al., 2011), particularly those that are high on episodic detail (Spreng, et al., 2010). It is possible, for example, that trait levels of private self-consciousness may relate to particular aspects of mental life characterised by simulations of the future that contain high levels of detail, a perspective that is supported by studies that have shown priming self-relevant information increases an individual's tendency to consider events in the future (Smallwood et al., 2011). This is an important question for future research to address.

One limitation of our study is that we focused on a relatively coarse description of neural function that is characterized by a neural parcellation that divides the cortical landscape into seven large-scale networks. Recent accounts of the DMN suggest that it can be subdivided into different sub-networks (e.g., Yeo et al., 2011, Andrews-Hanna et al., 2010). One of these sub-divisions, known as the medial-temporal subsystem, encompasses regions of posterior parietal cortex, but critically aspects of the medial temporal lobe. It is therefore possible that a more fine-grained analysis of the relationship between DMN sub-networks at rest and different aspects of self-consciousness would have revealed a role for one of these subsystems. Although our coarse analysis revealed patterns of neural activity that described two out of three forms of self-consciousness it remains an open question whether looking at the behaviour of subsystems of the DMN at rest, or during tasks, may reveal a role for aspects of this large scale network in trait differences in self-consciousness. Notwithstanding this limitation, our current study suggests that trait variation in private self-consciousness is related to the functional connectivity of the FPCN, and in particular to its communication with regions involved in episodic memory retrieval. This pattern of functional connectivity moderates the association between private self-consciousness and a heightened memory for self-relevant information, identified by prior investigations. Together these findings suggest that a greater capacity for the retrieval of self-relevant information may explain important aspects of the processes through which we become the subject of our own conscious evaluations.

4.6 References

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Chapter 5 - General Discussion

5.1 Main Questions

The current doctoral thesis was aimed at exploring patterns of functional connectivity in the intrinsic architecture of the brain related to individual differences in self-bias. The first and second used the memorial advantage for self-related material as a potential measure of the degree of one's self-schema articulation, with the first study exploring how this measure related with functional connectivity of DMN regions classically involved in self-referential processing and the second one exploring how it related to regions of the FPCN. The selection of regions of the FPCN for the second study was based on a behavioural finding from the first study, that of a negative correlation between one's mnemonic advantage for self-related material and inhibitory control efficiency. The second study did not only replicate this behavioural finding, but also provided insight into its neural underpinnings using a cross sectional design: functional connectivity of regions involved in inhibitory control was explored in relation to the magnitude of the self-reference effect, and on a similar fashion, inhibitory control efficiency was used to predict the FC of regions involved in self-referential processing. The third study took an alternative measure of self-focussed attention using the self-consciousness scale devised by Fenigstein, Scheier & Buss (1975) and explored the functional connectivity of both the DMN and the FPCN.

5.2 Summary of findings

The first question of the current work was whether the functional connectivity of regions involved in self-referential processing was predictive of the magnitude of the self-reference effect. The self-reference effect was assumed to capture the degree to which an individual has developed their self-schema, a process thought to involve self-focussed attention. The functional connectivity of regions in the mPFC, classically involved in self-referential processing was explored in relation to the magnitude of the self-reference effect and a common pattern emerged from the results: a stronger self-

reference effect was related to stronger functional connectivity within the DMN. The DMN is assumed to be involved in internal representations and as such is tightly linked to memory. Different subsystems exist within the DMN, one being involved in episodic aspects of memory, another one in semantic ones (Andrews-Hanna, Smallwood & Spreng, 2014). Our results mainly revealed that a stronger interaction between these two systems was related to a stronger self-reference effect, a pattern that has previously been related to increased mind wandering (Poerio et al., 2017).

Another important question we set to answer was whether there was a relationship between the magnitude of the self-reference effect and inhibitory control. The rationale for this was based on the salient properties of self-relevant material. Salient stimuli act as powerful distractors (Theeuwes, 2010), and hence we hypothesised that individuals with stronger self-reference effect would be less efficient at tasks that require sustained attention on the external world such as inhibitory control tasks, a finding that would suggest that the magnitude of the self-reference can be indicative of one's tendency to engage in self-focussed attention. This hypothesis was confirmed and replicated in study one and study two. Importantly, we explored the relationship between the functional connectivity of the FPCN and two measures of self-bias: the self-reference effect (study 2) and scores in the self-consciousness scale (study 3). We found that both of these measures predicted the functional connectivity of the FPCN. While the self-reference effect was predicted by the functional connectivity of this large-scale network to the basal ganglia (BG) and, in particular, the nucleus accumbens, private self-consciousness was predicted by stronger functional connectivity between the FPCN and a cluster in the fusiform gyrus that extended into the hippocampus. Similarly, the first study found that regions of the FPCN were more connected to regions of the DMN in individuals with smaller self-references effects caused through enhanced memory in the familiar other condition.

As we will discuss in the coming sections a pattern emerges in which stronger coupling between areas involved in executive control and self-representation results in a reduced self-reference effect, whereas enhanced functional connectivity between memory related areas involved in self-representation results in heightened mnemonic advantage for self-items. In particular, a reduced self-reference effect was related to

increased coupling between the FPCN and the nucleus accumbens, a central region of the reward system highly related to value-signalling and hence, self-relevance (Study 2). Reduced magnitude of the self-reference effect, caused by increased memory for the unfamiliar-other condition, was also related to stronger coupling between regions of the FPCN and the vmPFC (Study 1). When instead the vmPFC coupled to regions in the DMN individuals presented a stronger self-bias caused by both an increased memory for self-items and a decreased memory for items in the unfamiliar-other condition. A summary of the patterns of functional connectivity related to self-focused attention can be found in Figure 5.1.

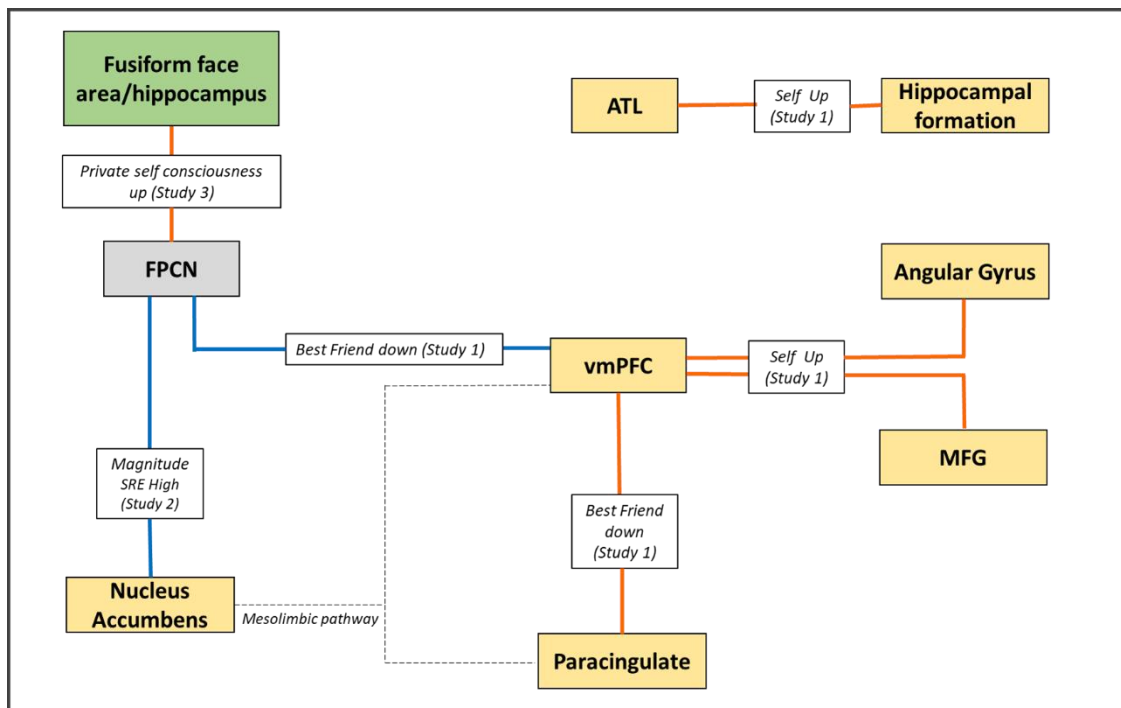


Figure 5.1: Summary figure reflecting patterns of functional connectivity related to self-focused attention. The blue lines represent reduced coupling, the orange lines represent increased coupling, the dotted lines represent connections defined previously in the literature (Meredith & Totterdell 1999). The yellow boxes represent regions in the Default Mode Network. The boxes situated between the lines represent the behavioural outcome that was associated with the pattern of functional connectivity depicted by the particular line. ATL: Anterior Temporal Lobe; FPCN: Frontoparietal Control Network; MFG: Middle Frontal Gyrus. Mesoli

5.3 The Relationship between the DMN and the SRE

Self-focussed attention emerges as an interplay between a semantic representation of self and episodic memory that allows an individual to, for example, revise one's behaviours. In other words, engagement in this processes requires a point of reference in which one's values or personality are activated and used to make decisions or judgements. Material related to the self has repeatedly been shown to be encoded better than other types of material (see meta-analysis by Symons and Johnson 1997). This is in part due to the vast network of associations related to the self which, by creating extensive memory traces, aids retrieval. This is further enhanced thanks to the activation of the self-schema during encoding. Following previous research suggesting memory performance is related to elaboration processes and to schema-activation we assumed that a stronger memorial advantage for self-related material would be indicative of the degree to which someone has developed their self-schema, in turn potentially reflecting an individual's tendency to engage in self-focussed attention.

Having obtained a potentially objective measure of self-focussed attention, we explored whether this measure was predictive of the intrinsic architecture of regions in the brain involved in self-referential processing. Self-referential processing has been related to activations in the DMN (see meta-analysis by Northoff et al., 2006), with particular consistency in the most anterior aspect of this network, i.e., the mPFC. This result was replicated in the second study in the current doctoral thesis in which a localiser task comparing activation during self-reference versus activation during other reference revealed the mPFC. Previous research has revealed this area to be particularly involved in the enhanced memorial properties of self-relevant material, with stronger activations during processing of self-referenced items resulting in enhanced subsequent retrieval of such items (Kelley et al., 2002; Macrae, Moran, Heatherton, Banfield & Kelley, 2004). Other areas such as the parahippocampal cortices and the left anterior prefrontal cortex were also involved in heightened encoding of self-relevant material, however these areas seem to have a more domain general and verbal role in encoding, respectively (e.g., Aguirre, Detre, Alsop &

D'Esposito, 1996; Fernandez et al., 1998; Li, Lu, Li & Zhong, 2010; Rombouts et al., 1997; Stern et al., 1996; Wagner et al., 1998) suggesting only the mPFC to be specific to the self-reference effect. Based on these findings, the first study explored how the functional connectivity of several regions of the mPFC related to the magnitude of the self-reference effect.

The first study revealed that stronger self-reference effect was related to heightened coupling between the mPFC to other regions of the DMN, a network classically involved in processing of internal representations (Spreng, Mar & Kim, 2009) which deactivates during processing of external stimuli (Raichle et al., 2001). This network is however not homogeneous, with clustering analyses revealing three different subsystems (Andrews-Hanna et al., 2014). The first empirical chapter found that a higher memory for self-related items was associated with stronger coupling between two of these systems. As revealed in an analysis that fractionalised the DMN into subsystems (Andrews-Hanna et al., 2014), different portions of the mPFC belong to different subsystems: the ventral mPFC is part of the medial temporal subsystem which also includes areas in the medial temporal lobes; the anterior mPFC is part of the core subsystem which includes the PCC; and the dmPFC, in combination with the angular gyrus and the lateral and frontal temporal lobes, form the dorsomedial prefrontal subsystem. Whereas nodes in the medial temporal and the dorsomedial subsystems present strong correlations with the core subsystem, the correlations between them is much lower, suggesting a segregation of functions (Andrews-Hanna et al., 2014). In particular, the dmPFC is involved in semantic processes (e.g., Andrews-Hanna et al., 2014; Mummery et al., 2000; Visser, Jefferies & Lambon Ralph, 2010; Visser, Jefferies, Embleton & Lambon Ralph, 2012) and the medialtemporal one on episodic processes (e.g., Andrews-Hanna et al., 2014; Nyberg, McIntosh, Houle, Nilsson & Tulving, 1996; Race, Keane & Verfaellie, 2011; Schacter & Wagner, 1999). For example, when subjects are asked to think about the self in an episodic way, such as when they are asked to think about where they will be tomorrow, activation on the medial temporal subsystem increases. Note that activation in regions of this subsystem such as the hippocampal formation and the parahippocampal cortex are also heavily involved in encoding and retrieval (e.g., Epstein, Harris, Stanley & Kanwisher, 1999; Epstein, DeYoe, Press, Rosen & Kanwisher, 2011; Hayes, Nadel &

Ryan, 2007), processes that interact with schemas held in semantic memory, accounting for why the vmPFC, highly involved in schema activation, belongs to episodic subsystem principally anchored in the medialtemporal lobes. Instead, when subjects are asked about a certain aspect of themselves, a process that relies more on semantic than episodic material, increased activation is found in the dorsomedial prefrontal subsystem (Andrews-Hanna et al., 2014). Additionally, areas in this subsystem, like the angular gyrus, are also involved in social cognition such as theory of mind or mentalizing (e.g., Calarge, Andreasen & O'Leary, 2003; Schurz, Radua, Aichhorn, Richlan & Perner, 2014; Seghier, 2013). Evidently, both subsystems strongly interact. For example, during introspection the semantic self has to be activated and revised when judging one's actions in a specific episode.

In relation to this, Study 1 found that a stronger coupling between the two subsystems, in particular between the ventral mPFC (episodic subsystem) and the angular and middle temporal gyri (semantic subsystem) was related to enhanced memory for self-related items. Note that, based on this subdivision of the DMN, the vmPFC is considered an important node of the episodic medialtemporal lobe subsystem. However, the vmPFC also has a well-established role during tasks that require engagement of schemas, thought to rely on semantic memory (Ghosh & Gilboa, 2014). Given the vmPFC's role both during self-referential processing, schema-based encoding and episodic memory, it is tempting to suggest that this area is involved in the semantic representation of the self and in particular in how this representation interacts with episodic memory. Importantly, the results suggest that an increased interaction between the episodic and the semantic subsystems is related to the enhanced encoding of self-related material. The increased interaction between both systems might be suggesting a heightened recruitment of the semantic self during the episodic reconstructions. It is possible that this heightened activation of the semantic self, and in particular through its interaction with the episodic information, would in turn lead to the increased self-bias related to this pattern of functional connectivity. Importantly, increased integration between both subsystems has previously been linked to mind wandering (Poerio et al., 2017), a process which highly overlaps with self-referential processing, as can be seen from previous

literature (Gusnard, Akbudak, Shulman & Raichle, 2011; Spreng et al., 2009) as well as the results from the self > other contrast obtained in the localiser scan in Study 2.

The discussion so far has argued that an increased memory for self items seems to be related to a stronger integration within DMN subsystems. Overall this higher integration between subsystems of the DMN results in a stronger within DMN synchrony. This result was similarly mirrored when exploring the memory for the non-self condition. In this case, stronger coupling between the vmPFC and the paracingulate cortex, embedded within the DMN, was observed in individuals with a reduced memory for the control condition measuring memory for best friend items. Note that the individuals with the highest self-reference effect will not only present the strongest memory for self items but also the weakest memory for the control condition, hence once again, stronger functional connectivity across DMN regions results in enhanced self-reference effects. Overall our results thus far suggest that a stronger self-reference effect is related to a hyperconnected DMN.

5.4 Self and Reward

The results from the second study might help us understand why certain individuals more commonly activate self-related systems than others. In this study functional connectivity analyses of the FPCN revealed that a reduced self-reference effect was related to stronger coupling between the FPCN and the ventral striatum classically involved in reward. A growing number of studies have shown a strong overlap between self-related regions, in particular those involved in assigning personal relevance to stimuli, and the reward system, shedding light on why this reward related region was obtained for analyses of the self-reference effect. Consistent activations during processing of self-specific stimuli have been found in classic reward system regions such as the ventral striatum and ventral tegmental area, as well as in the vmPFC (de Greck et al., 2008; Enzi, De Greck, Proesch, Tempelmann & Northoff, 2009; Ersner-Hershfield, Garton, Ballard, Samanez-Larking & Knutson, 2009). This is not surprising, as both self-specificity and reward rely on value-

assignment, i.e., self-relevant material is that to which the self has assigned either positive or negative value to. Similarly, one needs to activate the semantic self in order to make everyday judgements. For example, “Did I behave in a correct way?”, “Was Mary wearing too much makeup?”, “Should Adam apologise to Tom?” are all examples in which one needs to access the semantic self which holds the belief system of who we are in order to answer these questions. Further supporting the relationship between the reward/value assignment system and self-relevant stimuli, other studies have found that performance for self-related material mirrors that of trials with high-reward items, with both sorts of stimuli leading to an advantage during processing (Sui & Humphreys, 2015), an advantage possibly achieved through the effect both self and rewarding stimuli have over attentional resources. Hence, this close relationship between self and reward systems might account for why the functional connectivity of the nucleus accumbens, classically involved in reward processes, was found to be involved in the magnitude of the self-reference effect.

5.5 Within and Between Functional Connectivity of Self-Referential and Executive Control Regions: Relationship to the Self-Reference Effect

Whereas the nucleus accumbens is part of the reward system, and as such, is closely related to orbitomedial prefrontal cortex (Kringelbach, 2005), our functional connectivity results revealed that it was its coupling to the FPCN that was predicted by the magnitude of one’s self-bias. The ventral striatum, where the nucleus accumbens is located is part of the motivational corticostriatal loop, with the ventral striatum receiving strong projections from the orbitofrontal cortex. Another important corticostriatal loop is the executive loop connecting cortical regions involved in executive control such as the dorsolateral prefrontal cortex to the dorsal basal ganglia. Although these loops are highly segregated, recent research has shown that the corticostriatal circuits converge in the more rostral and ventral aspects of the striatum where the nucleus accumbens is located (Haber, 2016). Hence, since the

nucleus accumbens was obtained from seeding the FPCN, this pattern of functional connectivity seems to be indicating that a stronger integration between the executive and motivational corticostriatal loops is linked to a reduced self-reference effect. Considering that thinking about the self can be an automatic and even compulsive behaviour that results in a heightened self-bias, and that it is closely associated with the reward system, we turned to research on addiction to help us decipher why enhanced integration between the motivational and executive loops was related to a reduced self-reference effect.

A hallmark of addictive behaviour is an inability to suppress actions that lead to immediate reward in the pursue of a later reward. Whereas the reward system is active during immediate rewards, delayed rewards recruit regions like the dorsolateral prefrontal cortex involved in executive control (McClure, York & Montague, 2004). Neurologically, addiction is related to an imbalance between these two systems. Whereas the reward system is overactive, with individuals displaying enhanced reward sensitivity and increased synchrony within the reward system, the executive system shows reduced functional links (Dong, Huang & Du, 2011; Dong, Hu & Lin, 2013). Based on this imbalance, Dong, Lin, Hu, Xie and Du (2015) explored the functional connectivity of the reward and the executive control systems in internet gaming addicts, with a particular interest in the interaction between these two systems. Several seed regions in the reward and the control network were selected with the intention of exploring how the functional connectivity of the accumbens related to both systems. With special interest to the results obtained in the second empirical chapter, the authors found a negative correlation between the functional connectivity of the accumbens to the reward system and the functional connectivity of the accumbens to the control network in all subjects: as the functional connectivity of the accumbens to the FPCN increased, the functional connectivity of the accumbens to the rest of the reward system decreased, with this anticorrelation being more pronounced in gamers than in control subjects. Taking into account that the reward and the control system appear to compete for the functional connectivity of the nucleus accumbens, the stronger functional connectivity between the FPCN and the accumbens found in individuals with a reduced self-reference effect should also be related to a reduced functional connectivity between the accumbens and the other

regions of the reward/self system such as the orbitomedial prefrontal cortex. This reduced functional connectivity between main components of the reward system would be translated into a reduced synchrony within this system in subjects with reduced self-biases, which is the opposite of what is found in addicts. Similar to addictive behaviour, self-focussed attention is automated, can occur compulsively and can be hard to inhibit (Ingram, 1990). Importantly, previous research has shown that controlling mind wandering is linked to better delaying of gratification (Ruby, Smallwood, Engen & Singer, 2013). Hence, this pattern of functional connectivity linked to a reduced self-reference effect might be reflecting the mechanism by which one successfully suppresses compulsive self-referential processing, a process that in turn would have an impact on the magnitude of the self-reference effect.

Having found that a stronger coupling between regions that are highly connected to DMN regions (i.e., the accumbens) and regions in the FPCN resulted in a reduced self-reference effect, a similar pattern emerges when we consider the results for the best friend condition found in the first study. This study found that a stronger coupling between vmPFC and the FPCN resulted in better memory for the best friend items. If we consider the self-reference effect to be the difference between one's memory for self items and one's memory for items in the control condition, the individuals with an enhanced memory for the items in the control best friend condition will also be the ones with the smallest self-reference effect. Hence, taking this into account, a pattern emerges in which individuals with a reduced self-reference effect separate nodes that are commonly associated with the DMN, such as the vmPFC (study 1) or the accumbens (study 2), from the DMN and instead couple them to control regions in the FPCN.

Instead, a stronger self-reference effect is observed in individuals in which the DMN is hyperconnected to itself, a pattern that has previously been linked to poor executive control (Poerio et al., 2017). Note that the first study revealed stronger functional connectivity between the vmPFC and the paracingulate gyrus for individuals with worse memory for best friend items. Meta-analytic decoding of this cluster associated this cluster with terms such as "reward", "self-referential" or "value". Instead of coupling to the paracingulate gyrus, the vmPFC seed region from which this pattern of functional connectivity was obtained coupled more to FPCN in

individuals with better memory for best friend items as discussed previously. Hence, taking into account that the best friend memory relates to the magnitude of the self-reference effect, this dissociation in vmPFC's functional connectivity supports the notion that the relationship between reward and executive control plays an important role in an individual's self-reference effect magnitude.

5.6 Self-Focussed Attention and the Frontoparietal Control Network

5.6.1 Automatic and Controlled Processes Involved in the Self-Reference Effect

In support of this apparent competition between the DMN and executive control processes, the first and second studies both found that individuals with a bigger magnitude of the self-reference effect (calculated by subtracting memory scores from an unfamiliar-other condition from memory scores at a self-reference condition) were worse at inhibiting responses. This replication was found despite both studies used different inhibitory control paradigms as well as slightly different memory measures. During the retrieval phase the first study only tested participants on their familiarity for the items, whereas the second study included a source localisation phase, resulting in both studies measuring related but slightly different measures. Additionally, the first study used a stop signal response time task whereas the second one used a Go/No-Go task. Despite using different measures, the negative correlation between the magnitude of the self-reference effect and inhibitory control efficiency was found in both studies, suggesting this to be a robust relationship.

Some behavioural differences were however found. Whereas in both studies the magnitude of the self-reference effect correlated with inhibitory control, when the magnitude of the self-reference effect was broken down into the scores for self and the non-self memory control condition, scores in the non-self memory control

only correlated directly with inhibitory control in the second study, whereas in the first study only scores in the self condition correlated directly to inhibitory control. A potential explanation underlying the different relationship found across studies for the non-self control condition might be the different nature of the memory scores. Whereas the first study measured familiarity scores, the second study included a source localisation phase and only considered hits those words that had been encoded in detail, as proven by an accurate source localisation. The fact that only the second study found a direct correlation between incidental encoding scores in the unfamiliar-other control condition and inhibitory control suggests that inhibitory control is more strongly correlated with source memory than it is with familiarity memory in the case of the unfamiliar, non-self condition. Having said that, the magnitude of the self-reference effect, which takes this unfamiliar other condition scores into account, was much more strongly correlated with inhibitory control ($r = .426$, $p = .007$) than merely the memory scores for self-items in the first study ($r = .333$, $p = .038$). In addition, when the relationship between both memories was controlled for by including both self and unfamiliar-other memory scores as regressors in a linear regression model, a significant model ($F(2,36) = 4.8$, $p < .05$, $R^2 = .21$) was obtained in which both variables explained a significant amount of variance of the inhibitory control efficiency variable (self: *standardized beta* = .53, $t(36) = 3$, $p < .005$; unfamiliar-other: *standardized beta* = -.37, $t(36)$, $p < .05$). In particular, better inhibitory control was associated with both reduced familiarity memory for self-related items and with increased familiarity memory for items in the control condition, shedding light on how the memory for self-items and memory for non-self items is supported through different mechanisms: Whereas self-memory benefits from automatically orienting attention towards the self, memory for the other condition suffers and instead benefits from more controlled processes.

5.6.2 Thought suppression and the self-reference effect: Cancellation or Prevention?

The current doctoral work studied the relationship between tasks that require action inhibition and the self-reference effect. In the following section we discuss the

idea that the pattern of functional connectivity of the FPCN related to reduced self-bias might be understood with respect to thought suppression mechanisms. Importantly, the following section delves into different suppression mechanisms such as cancellation and prevention in an attempt to decipher, on light of the results obtained in the second study, which one of these two suppression mechanisms is potentially involved in the reduced self-reference effect.

The SSRT and GNG both measure action suppression and performance in both tasks is diminished in subjects with ADHD, a reason for which both tasks have commonly been used interchangeably as a measure of inhibitory control (Alderson, Rapport & Kofler, 2007; Dillo et al., 2010; Senderecka, Grabowska, Szewczyk, Gerc & Chmylak 2012; Wright, Lipszyc, Dupuis, Thayapararajah & Schachar, 2014). However, recent meta-analytic evidence suggests that these two tasks measure different aspects of inhibitory control: action cancellation and action prevention, respectively (Aron et al., 2007; Guo, Schmitz, Mur, Ferreira & Anderson, 2018). In the SSRT all trials are Go trials, i.e, an action is being prepared in every trial and only after having started preparing the action is one indexed to cancel it through a beeping sound. The SSRT therefore measures efficiency at action cancellation. Instead, in the GNG the Go trial stimuli differ in colour from those in the No-Go trials, therefore, if close attention is being paid on a trial by trial basis, there should be no action initiation in the presence of the No-Go colour and in turn action prevention, instead of action cancellation, should be present. Despite these differences might appear subtle, evidence supporting that these two tasks rely on different processes is presented in a meta-analysis performed by Guo and colleagues (2018). Comparing neuroimaging data of both tasks the authors found no overlap in brain activation between the SSRT and the GNG. Whereas the GNG recruited the left putamen, the SSRT was related to activation in the right caudate, among other cortical regions.

Inhibition has mostly been researched in terms of action inhibition, however semantic inhibition is also a fundamental aspect of appropriate cognition and executive control. For example, research on semantics suggests that in order to retrieve words that are only weakly associated with a specific term, one must inhibit those words which are highly associated with it (Levy & Anderson 2002; Rafal & Henik,

1994). This is because highly associated words can act as distractors, impeding access to the weaker ones. Hence, controlled suppression of the automatic associations is a fundamental aspect of semantic control and one that is disrupted in semantic aphasia, a disorder characterised by an inability to access weaker associated items without the help of cues that aid such retrieval (Jefferies & Lambon-Ralph, 2006). A situation depicting this that we can all relate to is trying to recall someone's name. If for some reason, for example similar phonetics, another person's name comes to mind, this erroneous name can cause great interference and disrupt access to any other names. Equally so, if one is trying to focus on a certain task but keeps thinking about the plans for Friday night, task performance will likely be negatively affected. Suppression of the most highly associated or more salient information is therefore fundamental when tasks require our focus and it is this aspect of inhibition that we believe accompanies a reduced self-reference effect. Despite the current doctoral work has used tasks that measures action inhibition we will now present some evidence that suggests thought and action suppression share some mechanisms.

In order to study the relationship between thought and action suppression Guo and colleagues (2018) included data of a Think No Think (TNT) task in their meta-analysis including data obtained from the GNG and the SSRT paradigms. The TNT has been used with the intention to measure one's ability to suppress thought. In this paradigm subjects first have to learn pairs of words until they can remember them to a certain degree of accuracy. Subsequently, subjects are presented with one of the words in the pair, and depending on the colour of the word, they either have to remember the associated pair or suppress it from entering consciousness. In order to measure the suppression performance memory tests are completed at the end with the idea that those words that had had to be suppressed were recalled less than those that had to be recalled. The meta-analysis searched for the neural correlates of this task during thought suppression and compared them to those obtained for the SSRT and the GNG. The authors found that the neural correlates of retrieval suppression obtained in the TNT task were the same as those obtained for the SSRT leading the authors to conclude that thought suppression in the TNT was achieved through thought cancellation rather than through thought prevention.

The functional connectivity results of the FPCN related to the self-reference effect found in study 2 however revealed a cluster located in the left accumbens and putamen that resembled more the meta-analytic results found for the SSRT than for the GNG. A potential explanation for this is the nature of the TNT task used in the meta-analysis. In this task subjects first learned a pair of words. When later shown one of the words in the pair they were asked to inhibit it. If the word pair has been deeply encoded, it is possible that exposure to one of the words automatically leads to the activation of the other word. Whether this automatic activation is avoided or whether it is only suppressed after it has occurred is a confound that the TNT used in the meta-analysis did not address. To overcome this confound, Guo (2017) conducted an fMRI study of the TNT task in which they included intrusion ratings of the associated pair. After excluding from the test phase all pair-associates that had not been properly encoded, trials in which intrusions were not reported were considered to have been governed by prevention processes whereas cancellation processes were assumed to be engaged during trials in which intrusions were reported. The authors found that downregulation of the hippocampus was associated with efficient retrieval suppression and dynamic causal modelling analyses revealed that this was achieved through a dlPFC-BG-hippocampus pathway. In particular, intrusion reduction was correlated with the dlPFC-BG coupling in such a way that a stronger coupling between these two regions resulted in a more pronounced intrusion reduction, resembling the pattern of functional connectivity related to a reduced self-reference effect in the second empirical chapter of this thesis and suggesting thought prevention to be responsible for the reduced self-reference effect. Furthermore, the results revealed that both retrieval prevention and retrieval cancellation were marginally anticorrelated with BG-hippocampal coupling, supporting previous research suggesting that the BG and the dlPFC play an important role in the downregulation of the hippocampus (Benoit, Hulbert, Huddleston & Anderson, 2014; Benoit, Davies & Anderson, 2016; Gagnepain, Hulbert & Anderson, 2017; Levy & Anderson, 2012). Overall these findings strongly suggest that the magnitude of the self-reference effect used in the current doctoral work is indicative of one's ability to suppress intrusive thought. Furthermore, the results from these studies suggest that the aspect of inhibitory control efficiency that is related to reduced memorial advantage for self

memory found in the current doctoral work resembles that of thought prevention rather than that of thought cancellation and that this process is achieved through BG downregulation of the hippocampus triggered by BG-FPCN coupling.

5.6.3 The Frontoparietal Control Network and Private Self-Consciousness

Further evidence suggesting an important role of executive control processes and self-focussed attention was found in the third study. In this study an alternative measure of self-focussed attention was used. Instead of using the memory scores for self and other related material the functional connectivity of large scale networks was explored in relation to a self-reported measure of self-focussed attention measured through the self-consciousness questionnaire. This study found that the functional connectivity of the FPCN and not the DMN predicted the degree to which an individual engaged in private self-consciousness. The private subscale of the self-consciousness questionnaire asks individuals to for example rate how often they reflect upon their feelings, behaviours or motifs, ultimately measuring the degree to which an individual engages in introspection. Previous research has repeatedly found that one's memorial advantage for self-related material is correlated with one's tendency to think about one's self, as measured through the private self-consciousness scale (Agatstein & Buchanan, 1984; Nasby 1985). Having explored how the functional connectivity of regions of the FPCN and several regions of the mPFC and hippocampal formation, located in the DMN and Limbic networks as defined by Yeo and colleagues (2011), were related to the magnitude of the self-reference effect, the third study used the self-consciousness scale as an alternative measure of self-focussed attention to explore how the patterns of functional connectivity of these networks related to this subjective measure of self-focussed attention. Surprisingly, the DMN didn't reveal any patterns of functional connectivity predictive of self-consciousness. This was not the case for the FPCN, for which increased functional connectivity to an area of the medial temporal lobes was related to increased private self-consciousness. Despite neurocognitive decoding of this cluster revealed terms such as "navigation", "objects"

or “encoding”, generally involved in processing of the external world, this cluster slightly overlapped with the hippocampus and was also related to terms such as “episodic memory”. Considering the role of the FPCN in working memory, an alternative but not mutually exclusive explanation is that the stronger coupling between the FPCN and this cluster in individuals with higher private self-consciousness could be indicating the increased time that these individuals spend revising their episodic memory, this being a prerequisite for private self-consciousness. During such revision, material from memory has to be kept in working memory, a process linked to the FPCN (Brunoni & Vanderhasselt, 2014), hence it is possible that this pattern of functional connectivity is reflecting the process by which the FPCN is manipulating information from episodic memory. Furthermore, this cluster was also related with terms such as “face” and embedded the right fusiform face area (FFA), particularly related to self-face processing. With special relevance to the current result, a study by Utevsky, Smith, Young and Huettel (2017) found that during social reward the functional connectivity of the FFA exhibited more coupling to the FPCN (relative to the DMN) suggesting that private self-consciousness might be motivated by future social reward.

5.6.4. Summary of the FPCN Involvement in Self-Focussed Attention

An overarching theme emerges from the results obtained in the three studies: The functional connectivity of regions involved in executive control located in the frontoparietal cortex is closely related to self-focussed attention. Whereas the second study found a pattern of functional connectivity to the ventral striatum possibly related to the suppressive role of the FPCN, the third study found a pattern of functional connectivity from FPCN to fusiform cortex extending into hippocampus possibly related to the role the FPCN plays in the maintenance of episodic information in working memory. Functional connectivity between the vmPFC and regions of the FPCN was also found in the first study in relation to the memory for the best friend in such a way that better memory for the non-self-referent was obtained when the vmPFC dissociated itself from the paracingulate gyrus, involved in reward processes,

and instead coupled to regions involved in working memory. Overall results suggest that stronger coupling between FPCN to reward regions that are commonly activated during self-relevance results in reduced self-reference effect.

5.7 Coupling between DMN and Salience network: Relationship to Go/No-Go efficiency

The current work hypothesised that there would be a negative relationship between the magnitude of the self-reference effect and inhibitory control. The rationale for this was based on the salient and hence distracting properties of self-relevant material by which, whilst having an enhancing impact on the self-reference effect, would interfere in sustained attention on the external world. After having explored the functional connectivity of inhibitory control regions in relation to the self-reference effect, a second analysis explored the relationship between inhibitory control performance and the functional connectivity of regions involved in self-referential processing.

The results revealed that an enhanced functional connectivity between the self-referential regions and the right inferior frontal gyrus was predictive of better inhibitory control. Further functional connectivity analyses of the right inferior frontal gyrus revealed this cluster to be part of the salience network and meta-analytic decoding related it to terms such as “inhibition response” and “stop signal”. It is important to note that although the right inferior frontal gyrus has commonly been related to inhibitory control processes (Aron, Robbins & Poldrack, 2004), activation in this region has also been found in cases in which no response inhibition was required. For example, Hampshire, Thompson, Duncan and Owen (2009), found that this region was recruited when important cues were presented regardless of whether a response was required. Their findings suggest that its previous association with inhibition tasks might have been driven by cue detection processes rather than by inhibition per se. In particular, the salience network, through its close relationship with interoceptive signals processed in the insula (Craig & Craig, 2009; Menon & Udin, 2010), is involved in the detection of stimuli that are salient to the individual (Perini et al., 2018). In the

case of laboratory tasks, as long as the individual is willing to engage in the task, the presentation of target cues should be processed as salient. In turn, this salience detection will redirect attentional resources according to the task demands in order to perform efficiently. However, if there is a failure at detecting the cue, subsequent performance in the task will be impaired. This interpretation would still account for why both transcranial magnetic stimulation and lesions in the right inferior frontal gyrus have been related to reduced efficiency at inhibitory control tasks (Aron et al., 2004; Aron, Robbins & Poldrack, 2014; Chambers et al., 2006).

The role of the salience network in directing attentional resources in accordance to the task has been demonstrated through both dynamic causal modelling (Goulden et al., 2004) and granger causality (Sridharan, Levitin & Menon, 2008) analyses. Both methods replicated the same findings: the salience network plays a causal role in switching between networks, particularly through suppressing the DMN and activating the FPCN (Menon & Udin, 2010; Sridharan et al., 2008). Furthermore, aberrant functioning of these three networks is involved in many psychopathological states (Menon, 2011). Hence, the pattern of functional connectivity found in which stronger coupling between the DMN and the salience network is involved in better performance at the GNG further supports the notion that appropriate interaction between these networks is a fundamental aspect of efficient cognition. In particular, our results, which reveal that stronger functional connectivity between DMN regions and salience network is involved in better inhibitory control, suggests that increased coupling between the DMN and the right inferior frontal gyrus is involved in the mechanisms which, through allowing the salience network to deactivate the DMN, result in higher inhibitory control efficiency.

How does the impaired interaction between these three networks relate to psychology? What is motivating the excessive salience of self? These are questions that will have to be addressed in future studies, however previous literature on the right inferior frontal gyrus invites us to speculate about the role social cognition might be playing in the relationship between self-focussed attention, inhibitory control and the appropriate interaction between these networks. Eisenberger, Lieberman & Williams (2003) have shown that social rejection activates a region that overlaps with

the right IFG cluster found in the DMN analysis linked to inhibitory control efficiency. Moreover, social information is high in emotional content, known to be a powerful distractor (Dolcos & McCarthy, 2006; Mueller, 2011) and Levens & Phelps (2010) have implicated both the insula and the inferior frontal cortex in resolution of such emotional interference. This evidence suggests that this region is highly involved in interference resolution caused by emotional and socially relevant stimuli. As social animals, information about our reputation is valuable and hence should be signalled as salient, recruiting systems involved in self-evaluation and perspective taking anchored in the DMN. Hence, acquiring a good reputation can act as a strong incentive. In fact, the same system involved in monetary reward is recruited during socially rewarding cues (Izuma, Saito & Sadato, 2008), including the insula. Building on such previous literature and on the results of the current doctoral thesis, a hypothesis to be tested in future studies is whether social reward is related to the patterns of functional connectivity found in the current work linked to self-focussed attention and inhibitory control.

5.8 Concluding remarks

The current work explored the relationship between different measures of self-bias and patterns of functional connectivity in the brain. It explored the self from a mnemonic and an attentional perspective by studying the degree of an individual's self-bias as measured by 1) the magnitude of self-reference effect (Study 1 and Study 2) and 2) private self-consciousness (Study 3) and relating these measures to the intrinsic architecture of regions involved in 1) self-representation supported by memorial mechanisms (Study 1 and Study 3) and 2) regions involved in executive control (Study 2 and Study 3). The results revealed that the magnitude of the self-reference effect and the scores on the private self-consciousness, despite correlated, differ. In particular, the patterns of functional connectivity obtained from the FPCN suggest that whereas the magnitude of the self-reference effect seems to be capturing an individual's tendency to suppress automatic retrieval of information (Study 2) in the form of self-focussed attention, the private self-consciousness is revealing a pattern of functional connectivity that might be representative of when retrieval of

self-related material is not suppressed and is instead manipulated in working memory (Study 3). Further research will have to confirm this interpretation by using methods of psychophysiological interactions that explore functional connectivity during tasks that monitor self-focussed attention or self-focussed suppression. Ideally, such results would reveal stronger functional connectivity between the FPCN and the ventral striatum during instances of self-suppression, following results from Study 2. This pattern of functional connectivity would revert during self-focussed attention and in turn the FPCN would increase its coupling to regions involved in episodic memory representing the maintenance of episodic memory in working memory, following results from Study 3.

Whereas the DMN didn't reveal any patterns of functional connectivity involved in self-consciousness, a stronger self-reference effect was related to stronger coupling between episodic and semantic subsystems of the DMN (Study 1). This increased interaction supports the notion that as the semantic self interacts with episodic memory, as revealed by the patterns of functional connectivity obtained from the vmPFC, the self-schema gets revised, updated and elaborated resulting in a stronger self-reference effect.

The current work has:

- Provided the literature on self with a novel application of the self-reference effect by interpreting its magnitude as an indirect measure of self-focussed attention, an interpretation that was confirmed by the observed negative correlation found with efficiency at tasks that require external attention.
- Demonstrated that this measure is directly related to an individual's inhibitory control efficiency, furthering understanding on the powerful distracting properties of self-related material.
- Revealed patterns of functional connectivity of not only the DMN but also the FPCN that are related to ones' tendency to direct attention inwards.
- Left open questions about how and why two measures of self-focussed attention, that of the magnitude of the self-reference effect and private self-consciousness differ.

5.9 References

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List of Abbreviations

ADHD	Attention Deficit Hyperactivity Disorder
amPFC	Anteromedial Prefrontal Cortex
BG	Basal Ganglia
dIPFC	Dorsolateral Prefrontal Cortex
dmPFC	Dorsomedial Prefrontal Cortex
DMN	Default Mode Network
ERP	Event-related potential
FFA	Fusiform Face
FC	Functional Connectivity
FPCN	Frontoparietal Control Network
GNG	Go/No-Go
HF+	Hippocampal Formation
IPS	Intraparietal Sulcus
LpSTS	Left posterior Superior Temporal Sulcus
lvATL	Left ventral Anterior Temporal Lobe
mPFC	Medial Prefrontal Cortex
OFC	Orbitofrontal cortex
rMTG	Right Middle Temporal Lobe
rSMG	Right Supramarginal Gyrus
SCS	Self-consciousness Scale
SSRT	Stop Signal Response Task
vmPFC	Ventromedial Prefrontal Cortex

