University of Ottawa Faculty of Medicine

Neural mechanisms of individuality – EEG studies in self and morality

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Contents

Preface

The experimental paradigm was designed by A Wolff and G Northoff, with input from M Constantini, N Wagner, and L Jurkovic. The pilot study, the full experimental study and all data analysis was completed by A Wolff, with supervision and direction by G Northoff. Ideas for analysis and feedback on results was provided by J Gomez-Pilar, T Nakao, Z Huang, and A Longtin.

The manuscripts for articles one and two were written by A Wolff, while the manuscript for article three was written by A Wolff and D Di Giovanni with input on the introduction and discussion by G Northoff. J Gomez-Pilar and T Nakao provided feedback on manuscript one, J Gomez-Pilar and A Longtin provided feedback on manuscript two, and J Gomez-Pilar, Z Huang, T Nakao, and A Longtin provided feedback on manuscript three.

The study was approved by the Research Ethics Board of the Institute of Mental Health Research at the University of Ottawa (REB# 2009018). All work was done with their approval and according to their procedures.

All participants in the study provided written and verbal informed consent prior to study participation.

Abstract

The need for individual neural markers has been expressed in both basic and clinical neuroscience. To address this, we here designed a novel behavioural paradigm in which to test several measures as possible neural markers of individuality which distinguish participants from each other in how they perceive, feel and perform cognitive tasks. The individualized paradigm for consequentialist moral dilemmas was validated, showing variability across participants in thresholds and reaction times. Next, task-induced activity changes in EEG activity during the time interval of the Late Positive Potential (LPP) in alpha power, along with phase coherence early in the trial, correlated with reaction times and scores of subjective emotional distress. From these findings in study one, in study two we measured trial-to-trial variability (TTV) and found that the TTV index in the alpha and beta bands correlated with reaction time and prestimulus Lempel-Ziv Complexity. These findings, again in the alpha and beta bands, support alpha power during the LPP, variability quenching in these bands, and early intertrial coherence as markers of neural individuality. Finally, measures of scale-free activity in the resting state, along with others, and self-consciousness scale subscores as indices of the self were investigated. It was found that the power-law exponent, autocorrelation window, modulation index and electromagnetic tomography activity in two Default Mode Network areas correlated significantly with the Private subscore of the Self-Consciousness Scale only. These findings indicate that these resting state measures, along with activity in the DMN, may serve as markers of neural individuality in the brain's spontaneous activity.

Introduction

Context: Interindividual differences and their scientific importance

In attempting to characterize the mean of all participants in a population, many neuroscientific studies have failed to define anyone accurately (Ganis et al., 2005; Miller et al., 2012; Vindras et al., 2012; Seghier and Price, 2018). Differences between individuals may be considered noise or measurement error, and measures of central tendency, the mean in particular, can mask or cancel out differences between participants at the neuronal and behavioural levels.

Several recent studies, however, have sought explicitly to measure the differences between individuals at the cellular, network, and brain levels (Thompson-Schill et al., 2002; Ersner-Hershfield et al., 2009a; Miller et al., 2012; Parasuraman and Jiang, 2012; Sauce and Matzel, 2013; MacNamara et al., 2015; Reineberg et al., 2015; Finn et al., 2017; Jang et al., 2017; Seghier and Price, 2018). Many of these studies focused on the differences between individuals at the behavioural, mental and neuronal levels (Ganis et al., 2005; Ersner-Hershfield et al., 2009a; Miller et al., 2012; Reineberg et al., 2015; Ferri et al., 2015; Geerligs et al., 2015; Gonen-Yaacovi et al., 2016; Nakao et al., 2016; Arazi et al., 2017a; Finn et al., 2017; Haar et al., 2017). Within the neuronal level, distinctions between task-evoked activity, activity before stimulus onset (prestimulus) and spontaneous activity have further looked at distinctions between individuals (He, 2013; Ferri et al., 2015; Bai et al., 2016; Qin et al., 2016; Huang et al., 2017a).

In the individual we see the interaction of genetic (Derringer et al., 2010), psychological (Segalowitz and Dywan, 2009; Volkova and Rusalov, 2016), environmental (Gard et al., 2017; Barch et al., 2018; Lackner et al., 2018; Youssef et al., 2018) and biochemical

(Puglia et al., 2015; Lou et al., 2016; Marsman et al., 2017) factors, with the result being their behaviour (Parasuraman and Jiang, 2012). It has been suggested in recent studies on neural variability that both genetic and environmental factors influence interindividual variability in both brain structure and function (Chen et al., 2015; Arazi et al., 2017a, 2017b). When analyses are done only at the group level, for example in studies of psychiatric and neurological patients, however, these important between subject differences are concealed (Parasuraman and Jiang, 2012; Knott et al., 2013) and data related to mechanisms of the specified disease and symptom variation are lost (Seghier and Price, 2018).

Therefore, the broad aim of this doctoral research project has been to investigate the interindividual variability of EEG neuronal activity and how this relates to behavioural variability between participants in a healthy sample. This was investigated at three levels: in a moral dilemma task paradigm which examined task-evoked poststimulus activity; in the same paradigm with a focus on stimuli individualized to each participant compared to stimuli shared by all participants; and finally, in the spontaneous activity of the resting state.

Literature Review

Interindividual variability on the behavioural level - Moral paradigm

Behavioural characterization

One experimental paradigm that has shown variability on both behavioural and neural levels has been the moral dilemma (Strohminger et al., 2011; Manfrinati et al., 2013; Wang et al., 2014; Pletti et al., 2016; Capraro and Sippel, 2017; Laakasuo et al., 2017; Yang et al., 2017). Based on the iconic Trolley and Footbridge problems of Phillipa Foot

(Foot, 1978), previously these thought-experiments were unrealistic scenarios used to provoke moral attitudes in their readers in order to study moral intuitions and reasoning. Recently, however, the arrival of autonomous vehicles (AVs) on our roads have provided a real-life scenario in which to apply these dilemmas.

The ethical question in the context of driverless cars, broadly, is how to program them to respond to an emergency in which people will be killed. One approach being considered would be to program the vehicle to minimize harm, specifically to behave in a way to reduce the number of people injured or killed, and to maximize the number of people saved (Kirkpatrick, 2015; Greene, 2016).

A recent behavioural study found that most participants showed a preference for AVs that were consequential - they minimized the number of casualties (Bonnefon et al., 2016). Approval of the consequential behaviour of the AV varied with the number of lives saved, with approval increasing with the number of lives saved doing likewise (Bonnefon et al., 2016). When presented with one person saved by the killing of another by an AV, only 23% of participants agreed. When one hundred people would be saved by an AV killing one person, 76% agreed, though there was much variability between research subjects.

Since the publication of the ground-breaking neuroimaging study in 2001 (Greene, 2001) which suggested that cognitive and emotional processes are governed by two separate systems that can conflict, much research has been done on the behavioural, psychological and neurophysiological responses to the iconic Footbridge and Trolley moral dilemmas of Phillipa Foot (Foot, 1978). What was previously a largely theoretical debate on moral reasoning has now been complemented by empirical studies that measure the neural and behavioural correlates of moral reasoning in neuroscience (Young and Saxe, 2008; Dean, 2010; Shenhav and Greene, 2010; Sarlo et al., 2012; Chiong et al., 2013).

Focusing on two contrasting forms of moral reasoning - consequentialism[1] and deontology[2] - these neuroscientific studies have generally investigated the mental states involved in behavioural interactions between people in a moral context. Most of these studies have focused on the differences in the behavioural and neurophysiological responses to these two forms of moral reasoning (Greene, 2001; Greene et al., 2004, 2008, 2009; Bartels and Pizarro, 2011; Sarlo et al., 2014; Wang et al., 2014; Cellini et al., 2017). Few studies have compared deontology and consequentialist scenarios to non-moral reasoning (Greene, 2001; Greene et al., 2004, 2008, 2009; Chen et al., 2009; Bartels and Pizarro, 2011; Wang et al., 2014; Sarlo et al., 2014; Gui et al., 2015; Pletti et al., 2016; Cellini et al., 2017), and no neuroscientific studies have explicitly examined interindividual differences within consequential scenarios in which the ratios varied (Chen et al., 2009).

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1 Consequentialism - the normative (prescriptive) ethical view according to which the rightness or wrongness of moral judgements depends solely on the actions' consequences (Darwell *et al*, 2003). As such, consequentialism is close to what is also called utilitarianism. This moral theory reduces all morally relevant factors to consequences; neither the circumstances, nor the intrinsic nature of the act are instrumental as to whether an act is morally right or wrong.

2 Deontology - the rightness or wrongness of moral judgements cannot be justified by their consequences. Instead, some actions are intrinsically morally wrong (or right), no matter how good (or bad) their consequences are. What makes a moral judgement right is its conformity with a moral norm independent of the consequences.

Neural characterization

Most of this neuroimaging literature is comprised of fMRI imaging which is favourable for its high spatial resolution in detecting neural activity changes in specific regions or networks. In recent years, however, some researchers have embarked on investigating the temporal dynamics of moral reasoning using EEG and event-related potentials (ERPs). There has been a surge of interest in studying ERPs related to moral cognition and decision-making in general; both morally relevant decisions and morally irrelevant decisions have been studied (Chiu Loke et al., 2011; Sarlo et al., 2014; Yoder and Decety, 2014; Pletti et al., 2015).

Several ERP components have been linked to, and studied within, the context of moral decision-making. These can be roughly divided into early activity (50-200ms) such as the N100 (Cui et al., 2016; Gan et al., 2016; Wang et al., 2016), late activity, such as the P300 (Chen et al., 2009; Wang et al., 2014; Yang et al., 2014b; Yoder and Decety, 2014; Gui et al., 2015; Hundrieser and Stahl, 2016; van Noordt et al., 2016), or finally very late activity, such as the Late Positive Potential (LPP)(Yoder and Decety, 2014; Foucart et al., 2015; Zhang et al., 2015).

The early components are usually, although not exclusively, associated with automatic processes and modulated by physical, low-level properties of the stimuli (Haidt and Graham, 2007). The later components are usually seen as a product of higher-order cognitive processes (MacNamara et al., 2009; Weinberg and Hajcak, 2010). It has been shown, for example, that the early N200 component, a negative deflection occurring approximately 200ms after stimulus presentation, is larger for words reflecting a moral violation (not dependent on authority or rules) rather than a conventional (contingent on social constraints) violation (Lahat et al., 2013). This activity is usually considered a reflex of conflict monitoring and saliency processing – the automated orienting of perceptual and cognitive resources to sensory data (Botvinick et al., 2004; Harsay et al., 2012). The N200 is also reported to differentially react to fair and unfair proposals in the 'ultimatum game', an economic experiment in which participants must accept or reject the proposal of other participants regarding how to split a certain sum of money. Reactions to fair or unfair proposals have been interpreted as reflecting moral attitudes (Boksem and de Cremer, 2010).

Its has been shown (Yoder and Decety, 2014) that this early activity is modulated by pro-social and anti-social actions - higher amplitudes in the N1, N2 and LPP for prosocial actions compared to antisocial actions - pointing towards a very rapid classification of the emotional saliency of the presented moral scenarios. The involvement of very rapid differential processing of morally relevant stimuli has also been suggested (Sarlo et al., 2014), where the P260 component was shown to be sensitive to different dilemma-based scenarios. Furthermore, the modulation of the component was dependent on the individual scores of personal distress, indicating that the electrophysiological activity is sensitive to the unpleasantness of the decision-making process. The same component appears to be sensitive to the consideration of legal consequences of the actions, being larger in the case where they do not exist – indicating heightened affective conflict (Pletti et al., 2015). The authors have also shown how, in the condition where legal considerations matter, motor preparation is enhanced.

Despite the evidence for this very early modulation of stimulus processing based on the stimulus characteristics and experimental conditions, the same and other studies have also shown how the later processing, reflecting higher-level cognitive mechanisms, is involved in morally relevant scenarios. These include allocation of attentional resources to a stimulus (Polich, 2007), cognitive appraisal - evaluation of the stimulus following a set of rules - and re-appraisal (Decicco et al., 2012; Shafir et al., 2015) or even the processing of semantic content and the detection of incongruencies (Federmeier et al., 2007). Similar to the results found in the earlier components, the LPP, a positive deflection occurring after 300ms post-stimulus, appears to differentiate between pro-social and anti-social scenarios (Yoder and Decety, 2014) with a higher amplitude in the prosocial scenarios, and is sensitive to the type of scenario presented, being modulated by perceived unpleasantness (Sarlo et al., 2014).

These findings are consistent with previous studies demonstrating an N400 effect, typical of incongruence detection, to words inserted in objectionable statements in line with, or in conflict with, participants' reported values, followed as well by a modulation of the late positive potential (LPP) (Van Berkum et al., 2009). The same overall pattern of modulation of both early and late onset components by words in moral transgression scenarios' evaluation was found by Leuthold (Leuthold et al., 2014).

It seems clear that, regardless of the stimulus type, both early and later ERP components are modulated by different dimensions considered to be morally relevant. This favours the idea that moral cognition implies both automatic and very fast processing of presented stimuli as well as subsequent active appraisal and cognitive effort.

Open questions

Of the many recent studies which have examined ethical dilemmas (Young and Saxe, 2008; Dean, 2010; Shenhav and Greene, 2010; Chiu Loke et al., 2011; Sarlo et al., 2012, 2014; Chiong et al., 2013; Yoder and Decety, 2014; Pletti et al., 2015), no studies to date have examined explicitly inter-individual differences, at the behavioural and neural level, when parameters of consequential moral dilemmas are varied.

In contrast to ERP's, other measures in EEG such as the change in power across time - event-related spectral perturbation (ERSP), and phase-related processes as in intertrial coherence (ITC) - have rarely been investigated in EEG (Knyazev et al., 2016) during moral reasoning. One recent study did investigate the effect of moral engagement on alpha power (Petras et al., 2016), however this study used virtual reality as its stimulus, not the iconic Footbridge or Trolley dilemmas.

Interindividual variability on the mental level - Resting state and spontaneous activity

Neuronal characterization

The brain's resting state, or spontaneous activity, has been probed for its task-related and self-related relevance for almost twenty years (Raichle et al., 2001; Fox et al., 2006; Fox and Raichle, 2007; Schneider et al., 2008; Northoff and Hayes, 2011; Nakao et al., 2013a; Bai et al., 2016; Foster et al., 2016; Martino et al., 2016; Northoff, 2016a; Qin et al., 2016; Weiler et al., 2016; Huang et al., 2017a; Northoff and Huang, 2017). Recorded at rest in the absence of a task, it was found that a specific network, later called the default mode network (DMN), served as a baseline state for the brain with increased activity during the resting state compared to during a task (Raichle et al., 2001).

Since that initial finding, much research has been done to explore this resting state network and its relationship to task-evoked activity and psychopathology (Fox et al., 2006; Chiong et al., 2013; Lei et al., 2013; Mevel et al., 2013; Li et al., 2014; Raichle, 2015; Davey et al., 2016; Martino et al., 2016; Mohan et al., 2016; Northoff, 2016a; Qin et al., 2016; Huang et al., 2017a). The DMN can roughly be divided into three areas: the ventral medial prefrontal cortex, the dorsal medial prefrontal cortex and the posterior cingulate cortex (Raichle, 2015). The cortical areas of the DMN overlap with the cortical midline structures (CMS) and have been shown to be involved in self-referential processing and social cognition (Buckner et al., 2008; Northoff et al., 2011; Qin et al., 2016; Weiler et al., 2016; Huang et al., 2017a).

Mental characterization

The self has been much studied in neuroscience and is know to be associated with the CMS (Northoff and Heinzel, 2006; Murray et al., 2012, 2015; Sui et al., 2012). Several studies have found an overlap between activity in the CMS during the resting state and self-related activity (D’Argembeau et al., 2005; Qin and Northoff, 2011; Whitfield-Gabrieli and Ford, 2012; Davey et al., 2016; Huang et al., 2016; Qin et al., 2016) which suggests that spontaneous resting state activity contains information about the self. To measure the self at the mental level, the self-consciousness scale (SCS) (Fenigstein et al., 1975) and its Private subscale – concerns one’s inner thoughts and feelings (Fenigstein et al., 1975) - has been used in a previous study as an index of the self (Huang et al., 2016).

Open questions

Despite the previous study linking CMS activity to the self, this measurement, particularly in scale-free resting state measures, has not been done in the higher frequencies of neuroimaging that are accessed by EEG. In addition, no EEG studies yet have aimed to look at interindividual variability at both the neuronal and mental levels of the self.

Article 1: Behavioural and neural interindividual differences in task-evoked activity during a moral paradigm

Background and overview

Individualization was examined initially in a moral dilemma paradigm. The first article aimed to examine differences between participants at the behavioural and neurophysiological level on poststimulus, task-evoked activity.

In a tightly controlled healthy sample, we first designed a new experimental paradigm which varied the parameters of consequentialism. Since the morally relevant question in consequentialism relates to the outcome of the actions, and since the scenarios in the literature involve people being killed and saved, we varied the ratio of killed to saved. Specifically, after presentation of the scenario, the numbers of people killed and saved in the scenario were varied. Once a pilot study was completed, an EEG study was conducted in which the differences in behavioural and neurophysiological responses were examined owing to the variations in consequentialism.

The Footbridge was chosen over the Trolley scenario as it is a personal dilemma[3] that has been shown to increase brain activity in the ventral medial prefrontal cortex (vmPFC) and posterior cingulate gyrus, areas associated with emotional processing (Greene, 2001; Greene et al., 2004). In addition, previous studies have shown greater variability between participants in this scenario compared to Trolley-type dilemmas which have shown greater consensus (Youssef et al., 2012; Xue et al., 2013; Wang et al., 2014).

What then will be the neural differences between participants with different acceptable consequentialist ratios, and between this moral dilemma and a control condition?

In the first study, we aimed to determine if there was variability between participants on the behavioural measures. It was found that the threshold, reaction times, and emotional assessments of the scenarios showed differences between participants. After this finding, the next question was when during the time interval of the stimulus (2 seconds) did the ERP components with large interindividual variability that also had significant correlations with these behavioural measures fall?

As previously mentioned, most of the EEG studies on moral dilemmas have measured ERP activity (Chen et al., 2009; Chiu Loke et al., 2011; Sarlo et al., 2014; Yoder and

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[3] Personal dilemmas are variations of the Footbridge problem. A moral dilemma is classified as personal if the following three criteria are met: 1) it is likely to cause serious physical harm, 2) this serious physical harm must occur to a particular person of group of people, and 3) this serious physical harm cannot be a result of the deflection of an already existing threat onto a different person or group of people (Greene et al., 2004). These dilemmas are more likely to induce significant activity in emotion-associated regions such as the MPFC or the OFC (Harenski and Hamann, 2006). Impersonal dilemmas are those which do not meet the above criteria, and examples of these are variations of the Trolley problem. These dilemmas are more likely to induce significant activity in areas of cognition such as the parietal lobule (Han et al., 2014).

Decety, 2014; Pletti et al., 2015), while a few studies looked at band power in response to a stimulus (Laurentino et al., 2013; Knyazev et al., 2016; Petras et al., 2016). No studies, to date, have looked at the effect of moral dilemmas on phase coherence.

Aim

Therefore, our goal in this paper was to achieve three things. The first was to determine if there were differences between tasks in ERP activity in our new paradigm while the second was to examine how this neural activity related to our behavioural measures and when in the time course of the stimulus this occurred. Finally, our third aim was to apply infrequently used measures (ERSP, phase coherence through ITC and PLV) - with respect to the moral dilemma literature – to our paradigm and determine if there are differences between stimuli or conditions. After these questions were addressed, our final question asked which neural measures were best able to predict/disambiguate interindividual differences between participants.

Article 2: Trial-to-trial variability and information complexity as prestimulus mechanisms of neural individualization

Background and overview

The function and optimal range of ongoing neural variability in spontaneous activity (Pekny et al., 2015; Gonen-Yaacovi et al., 2016; Huang et al., 2018) has lately been deliberated (Dinstein et al., 2015). Its importance has been illustrated in motor activity (Pekny et al., 2015; Wolpert and Flanagan, 2016), however its extremes may be a contributing factor in several psychiatric illnesses or learning disorders (Milne, 2011; Dinstein et al., 2012; Hornickel and Kraus, 2013; Weinger et al., 2014; Yang et al., 2014a; Haigh et al., 2015; Saville et al., 2015).

Moreover, neural variability is considered a stable characteristic of an individuals' brain (Dinstein et al., 2015; Arazi et al., 2017b), and these interindividual differences in neural variability can be assessed by trial-to-trial variability (TTV) (Arazi et al., 2017a). TTV describes variance in response amplitude upon repeated presentations of the same stimulus and has been measured at multiple neuronal levels (Churchland et al., 2010, 2011; He, 2013; He and Zempel, 2013; Arazi et al., 2017a, 2017b). Prior to stimulus onset, one's ongoing spontaneous activity shows variability. Once a stimulus is presented, this variability decreases, or is 'quenched' (Churchland et al., 2010; He, 2013; He and Zempel, 2013; Schurger et al., 2015; Arazi et al., 2017b, 2017a; Huang et al., 2017a), but eventually returns to prestimulus levels. Since the stimulus in TTV is the same across trials, the variability in activity is a result of prestimulus and ongoing spontaneous activity fluctuations (Churchland et al., 2010).

Aim

For the second level of this work on individualization, this article focused on the effect of variability and prestimulus activity on stimulus evoked activity. The standard method of measuring neural responses in EEG and fMRI has been to average the responses over many trials (Friston et al., 1994) as was done here in the first article. This assumes, however, that the brain responds similarly to the stimulus over trials and can be extracted by averaging, thus suppressing the ongoing activity (He, 2013). It has been shown that variability in the response exists, and that variability interacts with the ongoing spontaneous brain activity (He, 2013; Huang et al., 2017a). The response variability has been shown to contain behaviourally relevant information (He, 2013;

Arazi et al., 2017a, 2017b) and provide additional information regarding neural activity after stimulus onset that averaged methods (ERP, ERSP) fail to measure.

Previous studies have shown that TTV is a stable feature of interindividual neural variability (Arazi et al., 2017b, 2017a), and a novel feature of our experimental design was the presentation to each participant of two individualized stimuli. Therefore, we investigated the effect of these individualized stimuli – across tasks – on poststimulus variability quenching as well as prestimulus spontaneous activity. The effect of individualization, through the individualized stimuli, was assessed on averaged methods such as ERP and ERSP, on the phase measure of ITC, and a variability measure over trials, namely TTV.

In addition, since previous studies have shown differential effects on frequency bands (Klimesch, 1999, 2011, 2012; Jokisch and Jensen, 2007; Jensen et al., 2010, 2014; Klimesch et al., 2011; Fellinger et al., 2011; Buzsáki and Silva, 2012; Buzsáki and Wang, 2012; Zumer et al., 2014; Bonnefond and Jensen, 2015; Petras et al., 2016), and from our alpha and beta results in the first article, we asked if differences between stimuli in TTV would be significant in the alpha and beta bands in particular.

Finally, we added further to the literature by introducing a measure of information theory, specifically Lempel-Ziv Complexity (LZC). The change of information (through complexity) with the arrival of the stimulus, and the effect of prestimulus complexity on poststimulus TTV, was measured. How does this information content, through the measurement of complexity, relate to TTV? Might it serve as a mechanism of neural variability quenching?

Article 3: Neural and mental Individualization - The brain’s spontaneous activity and its self

Background and overview

The investigation of individualization of spontaneous activity during the resting state is the aim of the third article. In this resting state study (all participants plus an additional 16 participants from an adjacent study to increase the sample size to *N* = 50), the self was used to index individuality and was operationalized through the use of the Self-Consciousness Scale (SCS) questionnaire (Fenigstein et al., 1975; Scheier and Carver, 1985). This scale has three subscores: Private, Public and Social. The Private subscale was used in this and a previous study (Huang et al., 2016) as a measure of the self.

The cortical midline areas of the CMS and DMN provide the link between moral decision-making, resting state activity, private self-consciousness, and possibly the individualization of stimuli (Schneider et al., 2008; Qin and Northoff, 2011; Davey et al., 2016). A previous fMRI study found that scale-free activity in areas of the DMN, specifically the mPFC and PCC, correlated significantly with scores of private self-consciousness, but no public or social self-consciousness (Huang et al., 2016).

Aim

In an attempt to 1) replicate the findings of the study by Huang et al. (2016), and 2) extend these findings in the higher frequency range of EEG and with additional measures, we correlated scale-free measures of the resting state with subscores from the SCS. The cortical areas examined here with source localisation, exact low resolution electromagnetic tomography (eLORETA), overlapped with the CMS area in the moral resting state paper (Han et al., 2016) which showed that these areas are also active in moral decision-making, and so vital for its function.

The analysis here complements the findings related to the moral dilemmas through its focus on cortical midline structures (CMS) and the default mode network (DMN). No studies have explicitly related private self-consciousness to moral dilemmas in the neuroscientific context (Moll et al., 2007; Stets and Carter, 2011; Reniers et al., 2012), however one recent study did examine the role of CMS in moral decision-making (Han et al., 2016).

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Article 1: Interindividual neural differences in moral decision-making are mediated by alpha power and delta/theta phase coherence

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Abstract

As technology in Artificial Intelligence has developed, the question of how to program driverless cars to respond to an emergency has arisen. It was recently shown that approval of the consequential behavior of driverless cars varied with the number of lives saved and showed interindividual differences, with approval increasing alongside the number of lives saved. In the present study, interindividual differences in individualized moral decision-making at both the behavioral and neural level were investigated using EEG. It was found that alpha event-related spectral perturbation (ERSP) and delta/theta phase-locking – intertrial coherence (ITC) and phase-locking value (PLV) – play a

central role in mediating interindividual differences in Moral decision-making. In addition, very late alpha activity differences between individualized and shared stimuli, and delta/theta ITC, where shown to be closely related to reaction time and subjectively perceived emotional distress. This demonstrates that interindividual differences in Moral decision-making are mediated neuronally by various markers – late alpha ERSP, and delta/theta ITC - as well as psychologically by reaction time and perceived emotional distress. Our data show, for the first time, how and according to which neuronal and behavioral measures interindividual differences in Moral dilemmas can be measured.

1. *Introduction*

1. *Interindividual differences in Moral preference – driverless cars illustrate its relevance*

Imagine you are riding in a driverless car. The car encounters a crossing, but for whatever reason cannot stop. Should the car sacrifice you, the passenger? Or should it sacrifice the ten pedestrians on the sidewalk? What would you as the owner of the car prefer? This Moral dilemma, previously a philosophical ‘thought experiment’ (Foot, 1978), has become an urgent public policy concern.

As of April 2, 2018, the state of California has allowed driverless cars on its roads; prior to that date, an approved person was required to sit in the driver seat to take control in case of emergency (Anon, 2018). With their arrival in our daily routines, the practicalities of driverless cars will add a layer of complexity to previously studied Moral dilemmas, specifically the Trolley and Footbridge problems (Foot, 1978).

Imagine you then pose the same questions to your friends and colleagues. They provide you with a variety of responses. The point on which there is the most divergence is the number of pedestrians for which they would be willing to sacrifice themselves as passengers. Two recent investigations showed that most participants prefer these consequentialist decisions – minimizing the harm by maximizing the number of people saved - in what the authors describe as an ‘emotionally salient’ situation (Bonnefon et al., 2016; Faulhaber et al., 2018). In addition, approval of the consequential behavior of the driverless car varied with the number of lives saved. Approval increased with the number of lives saved doing likewise but reached a maximum approval of 76% of participants. This, and other studies (Wang et al., 2014; Martin, 2017; Melnikoff and Bailey, 2018), demonstrate the central relevance of interindividual differences in Moral decision-making.

These interindividual differences revealed that participants are more consequential; they approve of actions in which the difference in numbers of saved to killed is small. Some, on the other hand, responded in a less consequential manner in that the ratio was larger. As other studies on Moral dilemmas show, the subjectively perceived emotional distress of the participant has a significant effect on their response (Manfrinati et al., 2013; Pletti et al., 2016) and reaction time (Manfrinati et al., 2013).

What, though, are the behavioral and neural bases for this interindividual variability in Moral preference? Many recent neural and psychological studies have examined ethical dilemmas (Chiu Loke et al., 2011; Sarlo et al., 2012, 2014; Chiong et al., 2013; Yoder and Decety, 2014; Pletti et al., 2015). None, however, have examined and tested explicitly for interindividual differences, at the behavioral and neural levels, within consequential scenarios in which the number of killed to saved varied. The closest study would be Chen, 2009 (Chen et al., 2009) which varied the relationships of participants in the scenarios within the relevant to participants' context of an earthquake. They found a higher amplitude of the P300 when the stress was increased when relatives were involved in the dilemma than when the other individuals were strangers. Interindividual variation of the Moral paradigms and their neural and behavioral effects remain unclear in current neuroscience. The aim of the current study, therefore, was to explicitly investigate the neural and behavioral correlates of interindividual differences in Moral preference.

2. *Moral decision-making – Neural correlates of interindividual differences*

Much research has been done on the behavioral, psychological and neurophysiological responses to the iconic 'Footbridge' and 'Trolley' Moral dilemmas of Phillipa Foot (Foot, 1978; Greene, 2001; Greene et al., 2004, 2008, 2009; Bartels and Pizarro, 2011; Sarlo et al., 2014, 2012; Chiong et al., 2013; Wang et al., 2014; Pletti et al., 2016; Cellini et al., 2017), though most of this is comprised of fMRI imaging. These studies have found that areas associated with emotional processing such as the medial frontal gyrus, the posterior cingulate gyrus and the bilateral angular gyri are more activity during Footbridge-like moral dilemmas than during Trolley-like dilemmas and non-moral dilemmas, while areas associated with working memory, such as the right middle frontal gyrus and the bilateral parietal lobes, are less active (Greene, 2001; Greene et al., 2004).

In recent years, some researchers have investigated the temporal dynamics of Moral reasoning using electroencephalography (EEG) and event-related potentials (ERPs) (Chiu Loke et al., 2011; Sarlo et al., 2014; Yoder and Decety, 2014; Pletti et al., 2015; Cui et al., 2016; Pasion et al., 2018).

A high temporal resolution may be central for detecting interindividual differences in Moral preference which manifest in the time course of neural activity. For this reason we chose EEG to investigate Moral preference (Chiu Loke et al., 2011; Sarlo et al., 2014; Wang et al., 2014; Yoder and Decety, 2014; Pletti et al., 2015). Most importantly, using EEG we examined interindividual differences through the individualizing of stimuli as well as through variation of the degree of consequentialism. The degree of consequentialism was varied by presenting participants with different ratios of killed to saved (one killed to save many, several killed to save many, number of people saved is only one more than killed, etc (Fig 1A-1).

3. *Aims and Hypotheses*

The main and overarching aim of our study was to investigate neural and behavioral correlates of interindividual differences in Moral preference. For that purpose, we designed a specific paradigm (Fig 1A) that, as based on the well-known Footbridge dilemma (Foot, 1978; Greene, 2001; Greene and J, 2002; Greene et al., 2004, 2008, 2009), allowed us to test interindividual differences in response to individually-tailored degrees of consequentialist decision-making.

Our specific aims were threefold. First, we examined the difference between the Moral and Control conditions, as well as between stimuli with varied ratios, through behavioral and ERP data. We hypothesized that late components (Chen et al., 2009; Chiu Loke et al., 2011; Wang et al., 2014; Yang et al., 2014b), specifically the Late Positive Potential (LPP), are related to interindividual differences in Moral preference as they are closely related to the processing of emotions (Brown et al., 2012; Hajcak et al., 2013; Minnix et

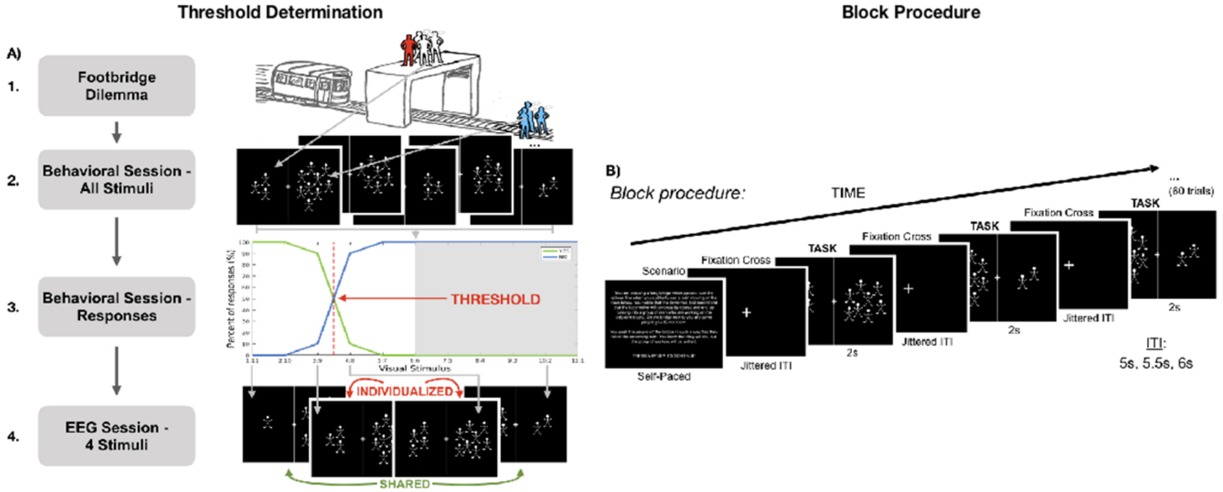

***Figure 1**: Study threshold determination block procedure. **A)** Determination of threshold in behavioral session. 1. Participants read a Footbridge-type dilemma in the behavioral session. Red: The participant in the scenario; White: the people that they would kill in the scenario; Blue: the people that would be saved in the scenario because they killed the others. 2. Participants were presented with 10 repetitions of each stimulus in a randomized order. 3. Based on the percentage of YES and NO responses for each stimulus in the preceding session, the threshold (dashed red vertical line) was calculated. 4. Finally, the stimuli immediately below and above the threshold - the Individualized stimuli - as well as two other stimuli Shared by all participants - 1:11 and 10:2 - were the only stimuli presented to participants in the subsequent EEG session. **B)** Block procedure for the behavioral and EEG session. The participant was presented one of three Footbridge-type dilemmas, which they read at their own pace. The trials were preceded by a fixation cross for a jittered duration of either 5, 5.5 or 6 seconds (randomized). The stimuli were a black screen with white two-dimensional stick people on either side of the screen, with a white line and fixation cross down the middle. The instructions given were that the people on the left side were those that would be killed in the previously read scenario, while the people on the right were those that were saved because of the others dying. Participants were instructed to respond either YES or NO (button randomly counter-balanced across participants) if the numbers of killed to saved presented in the stimulus were acceptable to them. The maximum duration of the stimulus was 2 seconds. In the EEG session, each block was comprised of 60 trials, with each stimulus being presented 15 times. ITI = intertrial interval.*

al., 2013; Moran et al., 2013; Babkirk et al., 2015; Burkhouse et al., 2015) which are core features of Moral preference (Leuthold et al., 2014; Yoder and Decety, 2014; Gui et al., 2015; Hundrieser and Stahl, 2016).

Secondly, in later ERP time intervals found to be have significant differences, differences in frequency band power were investigated, while phase coherence related to the stimuli was investigated in the full epoch. While no studies have investigated these neuronal measures in moral paradigms, several studies have demonstrated the central role of alpha ERSP and delta/theta ITC in mediating interindividual differences (Digiacomo et al., 2008; Csukly et al., 2014; DeLaRosa et al., 2014; Brooks and Kerick, 2015). We therefore hypothesized that alpha event-related spectral perturbation (ERSP) and intertrial coherence (ITC) in the delta/theta range would be central in mediating interindividual differences in Moral preference.

Finally, the relationship between the behavioral and the neural activity related to individualized and shared stimuli, frequency band power, and phase coherence will be determined. We hypothesized that interindividual differences in neuronal measures – LPP in individualized stimuli, alpha ERSP, and delta/theta ITC - during Moral decision-making are related to interindividual differences in both reaction time and perceived emotion. From this, we reasoned that interindividual differences in Moral preference are closely related to emotional arousal/perception as well as in their reaction time.

2. *Results*

1. *Reaction times were slower in the Moral condition and Individualized stimuli*

The behavioral data showed significant differences in reaction time in the Moral condition and in the Individualized stimuli near the threshold in all trials. A Wilcoxon signed-rank test showed that condition (Moral, Control) had a statistically significant effect on the reaction times in all trials (*Z* = -30.422, *p* < .000) (Fig 2B). Next, a Wilcoxon signed-rank test showed that proximity to threshold (Near Threshold, Far from Threshold) had a statistically significant effect on the reaction times in all trials (*Z* = -27.007, *p* < .000) (Fig 2B). Indeed, mean Near Threshold reaction time was 902ms while the mean for Far from Threshold stimuli was 763ms.

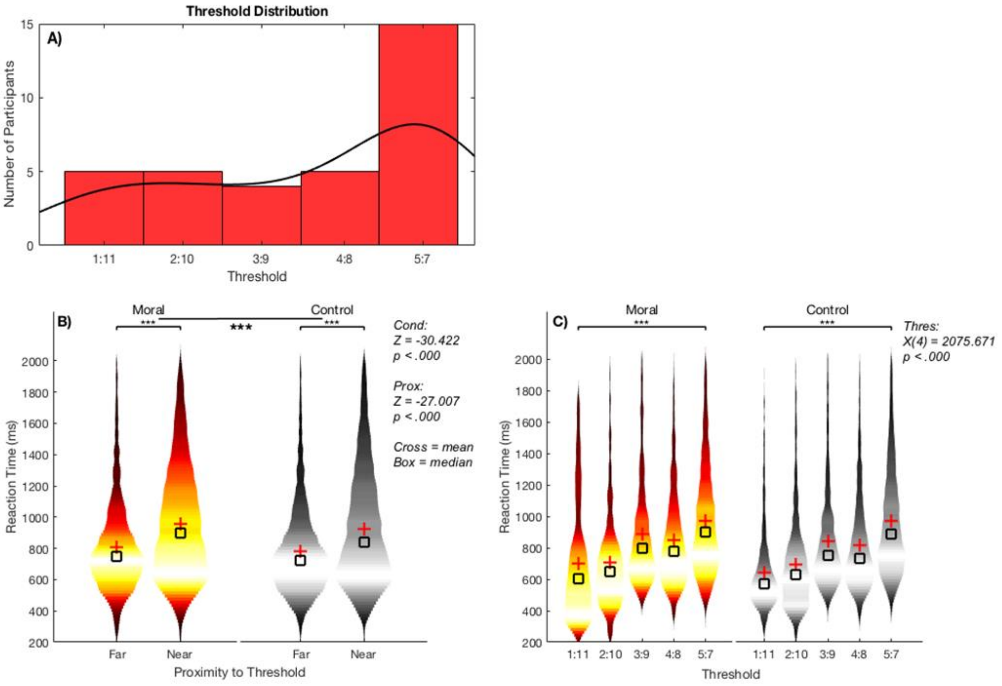

***Figure 2**: Threshold distribution and reaction time comparison between Moral and Control blocks in all trials. **A)** Distribution of thresholds of all participants. There was a roughly even distribution of participants in the lowest four thresholds, while the highest threshold, 5:7, contained the largest number. **B)** All trials in two Wilcoxon signed-rank tests measuring the effect of condition (Moral, Control) and proximity to threshold (Near, Far) on reaction time. There was a significant effect of both condition and proximity (Z-ratios and p-values stated). **C)** All trials in a Kruskal-Wallis H-test (5 levels) measuring the effect of threshold (1:11, 2:10, 3:9, 4:8, 5:7) on reaction time. Box = median, Cross = mean.*

Finally, a Kruskal-Wallis H test showed that there was a statistically significant effect of threshold on reaction time in all trials, $\chi^2(4) = 2075.671$, $p < .000$, with mean rank scores of the following: 1:11 = 3125ms; 2:10 = 3909ms; 3:9 = 5610ms; 4:8 = 5359ms; 5:7 = 6806ms (Fig 2C).

Therefore, reaction times were slower for the Moral condition, for Individualized stimuli, and in the more consequential thresholds.

2. Event-related potentials (ERP's) showed higher late activity in Individualized stimuli

The event-related potential (ERP) analysis found a significant effect of proximity to threshold in the N100, P300 and the LPP late time interval. For each time interval, a 2 (Moral, Control) x 2 (Near, Far) repeated measures ANOVA was performed on the maximum amplitude in the N100, N200 and P300 and the mean amplitude in the LPP.

In the early components, there was a significant main effect of proximity to threshold (Near, Far) in the N100 only (Wilks' Lambda = .747, $F(1,30) = 9.816$, $p = .004$), with the Near Threshold stimuli having higher peaks than stimuli Far from the Threshold (Fig 3A). There was no significant effect of condition (Moral, Control) in either the N100 or N200 (see Sup Mats).

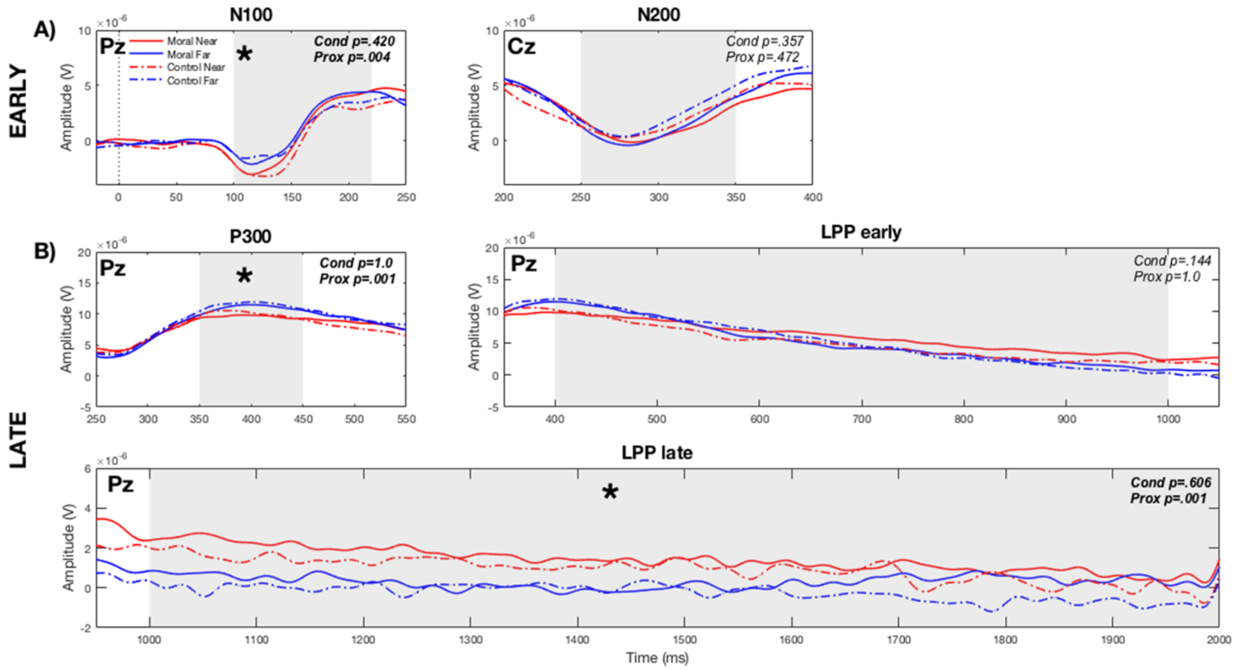

***Figure 3**: Event-related potentials (ERP's) of both early and late components. **A)** Early components. In the individual plots the data from Pz for N100 and Cz for N200 (see Methods) for each peak is illustrated, with p-values for condition and proximity to threshold stated. N100 had a significant effect of proximity, while neither condition nor proximity were significant for N200. **B)** Late components (at Pz). The P300 and the two time intervals for the LPP, with p-values for condition and proximity to threshold, are stated. In the P300, there was a significant effect of proximity to threshold, which was also true in the LPP late time interval. P-values stated.*

For the late components, there were significant effects of proximity to threshold (Near, Far) in the P300 (Wilks' Lambda = .675, *F*(1,30) = 13.964, p = .001) – higher peak amplitude in stimuli Far from the Threshold - and LPP late (Wilks' Lambda = .701, *F*(1,30) = 12.395, p = .001) time intervals (Fig 3B) which showed higher mean activity in stimuli Near the Threshold. In the LPP early time interval, there was a significant interaction between condition (Moral, Control) and proximity to threshold (Near, Far), (Wilks' Lambda = .858, *F*(1,30) = 4.795, p = .037).

In sum, activity from Individualized stimuli was higher than Shared in both early (N100) and late (LPP late) ERP components but lower than shared in the P300.

3. Moral alpha differed in event-related spectral perturbation (ERSP)

A significant difference in alpha (7-13Hz) band power was found in the LPP time interval between Near Threshold and Far from Threshold in the Moral condition only.

A paired-samples t-test, with the False Discovery Rate correction and a significance level of .05, showed a significant difference for the following times: between 8.2-11Hz from 430 to 680ms, 10.7-13.6Hz from 970 to 1000ms, 9.2-13.3Hz from 1000 to 1136ms, and 10.8-13.3Hz from 1471 to 1600ms (Fig 4). To ensure that the response activity had no effect on these findings, an ERSP time-locked to the response in each trial was done

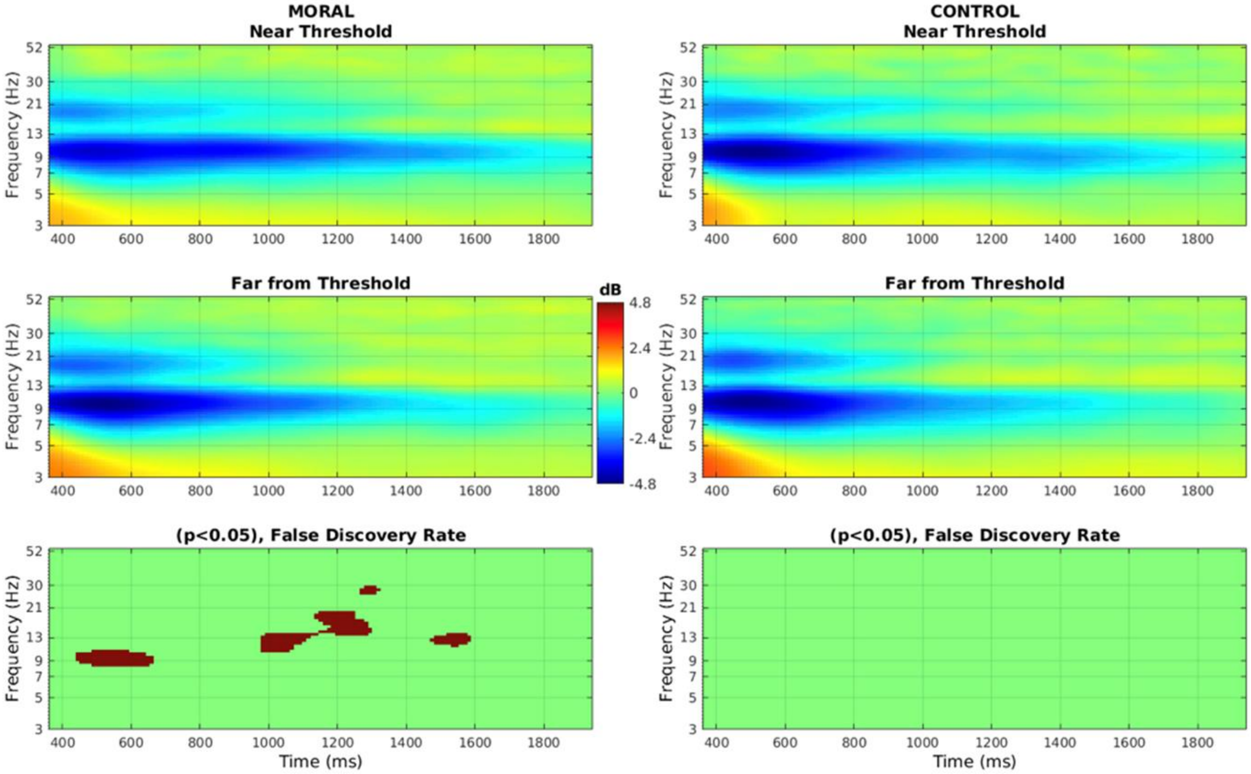

***Figure 4**: ERSP at Pz of late component in both conditions and for both proximities to threshold. Compared to baseline, there was a significant difference in Alpha (7-13Hz) and Low Beta (13-20Hz) in the Moral condition (left side) between the stimuli Near Threshold and Far from Threshold. In the same stimuli, there was no significant difference in the Control condition (right side). The significance level is .05, and t-tests are corrected for multiple comparisons using the False Discovery Rate.*

(Sup Fig 4). There was no significant difference between conditions related to response.

In sum, in the Moral condition there was a significant decrease in alpha power in the Far from Threshold compared to the Near Threshold stimuli in the later time intervals.

4. *Moral intertrial coherence (ITC) and phase-locking value (PLV) differed in delta/theta*

A significant difference was found in the Moral condition between Near Threshold and Far from Threshold in intertrial coherence (ITC).

A paired-sample t-test, with the False Discovery Rate correction and a significance level

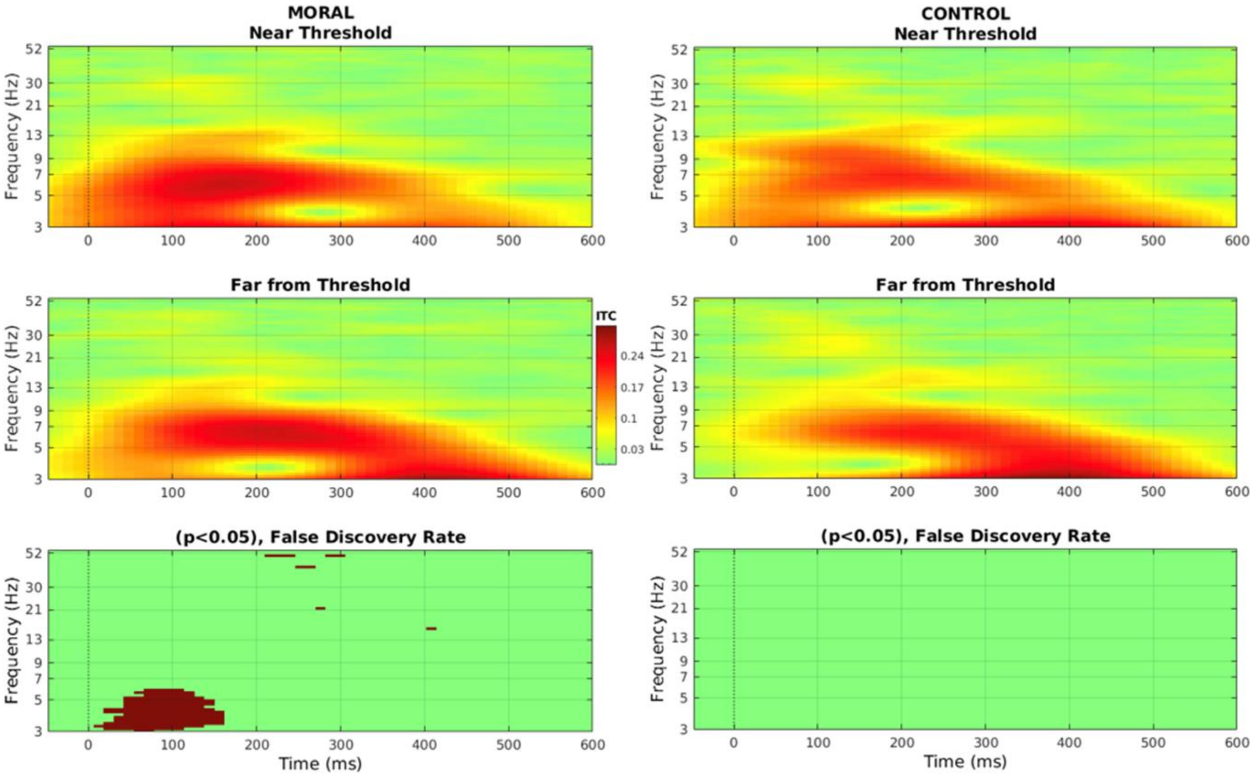

Figure 5: *ITC at Pz for the first segment of the epoch (0-600ms) in both conditions and for both proximities to threshold. ITC from baseline through stimulus onset (0ms) to 600ms for Moral (left side) and Control (right side) Near Threshold (top row) and Far from Threshold (second row). There was a significant difference in ITC from 3-6Hz in the first 150ms in the Moral condition. This was not seen in the Control condition. The significance level is .05, and t-tests are corrected for multiple comparisons using the False Discovery Rate.*

of .05, showed a significant difference between 3-6.1Hz from stimulus onset to 160ms (Figs 5, 6A), with increased ITC in stimuli Near the Threshold compared to Far from the Threshold. These differences were in the delta (1-4Hz) and theta (4-7Hz) band. Though these differences were in the slower frequency bands and the number of cycles was low, no such differences were seen in the Control condition.

After finding significant differences in the delta and theta bands of the ITC, the phase-locking value (PLV) for only these two bands were calculated to support the ITC

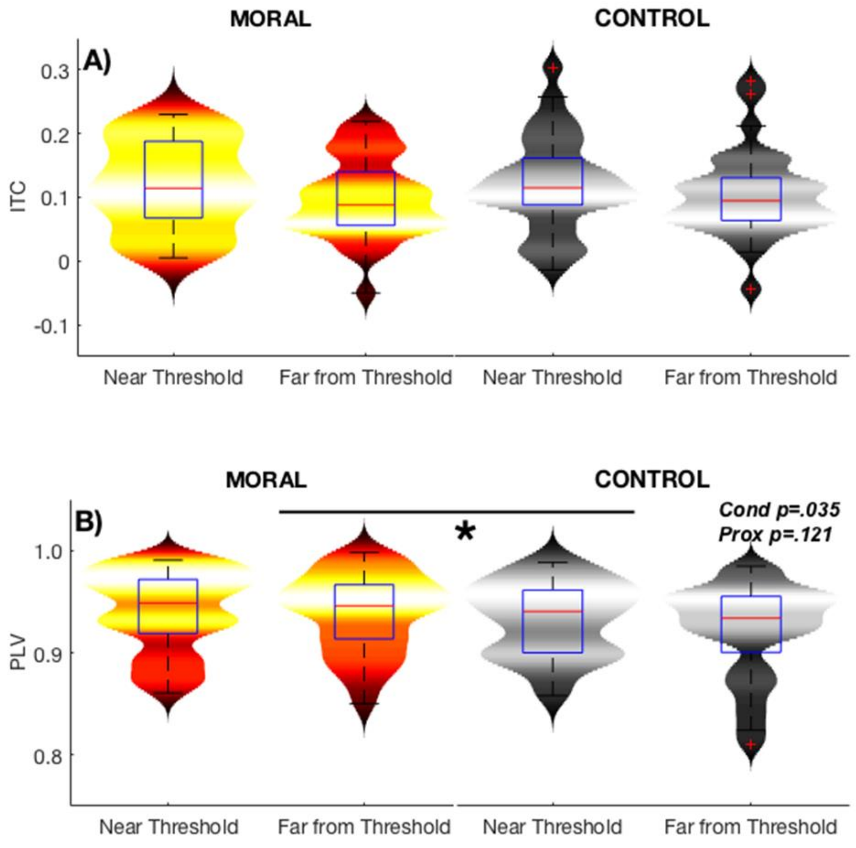

***Figure 6**: Intertrial coherence (ITC) and theta phase-locking value (PLV). **A)** A subset of ITC data, from 3-5Hz and between 0-100ms for both conditions and both proximities to threshold. This is for illustration of the data distribution only, therefore there are no statistics here as they were done previously in Fig 5. **B)** Theta (4-7Hz) PLV for the whole epoch (0-2000ms) in both conditions and both proximities to threshold. In the Theta band, there was a significant effect of condition (p-value stated) but not of proximity to threshold.*

findings. A significant difference in PLV was found in the theta (4-7Hz) band for the full interval (0-2000ms) in the Moral condition. A 2 (Moral, Control) x 2 (Near, Far) ANOVA showed a significant main effect of condition (Moral, Control) on theta PLV ($F(1,33) = 4.948$, $p < 0.035$) with higher phase-locking in the Moral condition, but not of proximity to threshold (Near, Far), ($F(1,33) = 2.563$, $p < 0.121$) (Fig 6B).

Taken together, delta/theta ITC showed significant increases in the Moral Individualized

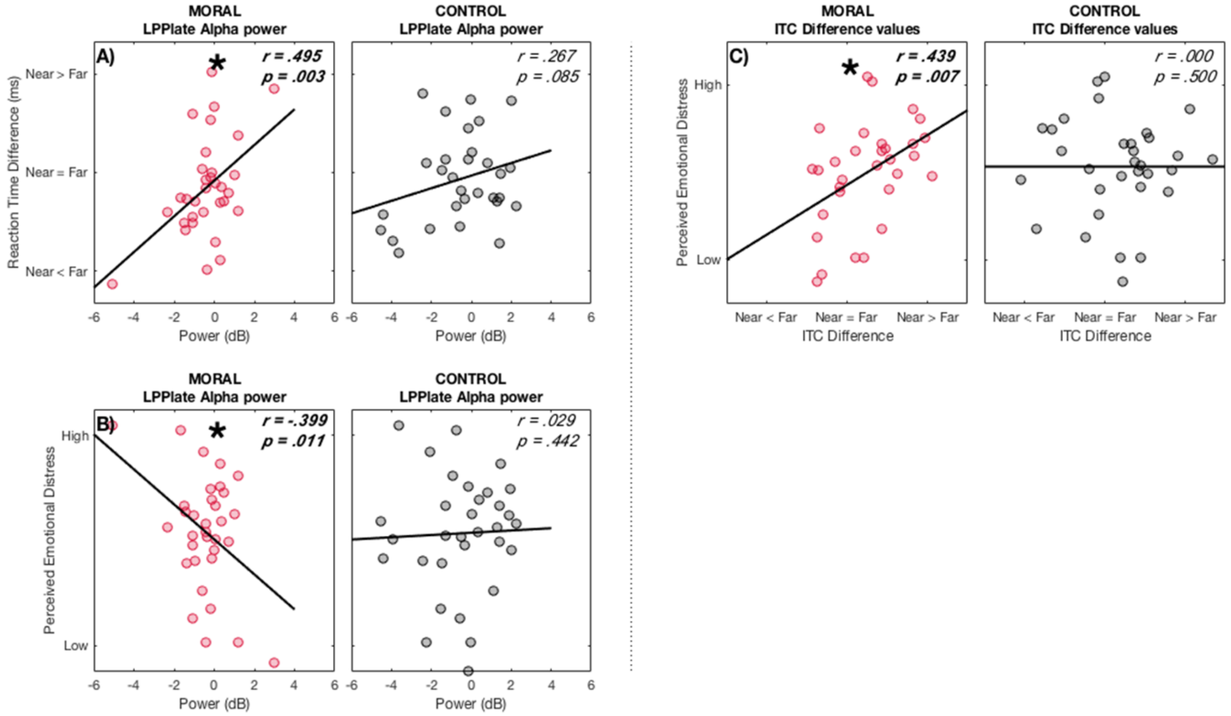

Figure 7**: Alpha power in the LPP late time interval and early intertrial coherence (ITC) and their correlations with reaction time (RT) and perceived emotional distress scores. RT, alpha power and ITC are difference values: Near Threshold values minus Far from Threshold values.* ***A) *Correlation of alpha power and RT difference in Moral and Control. The one-tailed, bootstrapped correlation was significant in the moral condition but not in the control condition.* ***B)*** *Correlation of alpha power and perceived emotional distress scores in Moral and Control. There was a significant correlation in the Moral condition, but not in the Control condition (r- and p-values are stated).* ***C)*** *One-tailed, bootstrapped correlations between ITC difference values and the perceived emotional distress scores. There was a significant positive correlation in the Moral condition, but not in the Control condition (r- and p-values stated). Red: Moral; Black: Control.*

stimuli while theta PLV in the whole epoch was significantly higher in the Moral condition compared to the Control condition.

5. *Alpha power is related to reaction times and subjectively perceived emotional distress*

The LPP late time interval had a significant correlation in alpha power with reaction times and the subjectively perceived emotional distress scores only in the Moral condition.

One-tailed bootstrapped correlations between alpha power and reaction time ($r = 0.495$, $p < 0.003$) (Fig 7A) and the subjectively perceived emotional distress scores ($r = -0.399$, $p < 0.011$) (Fig 7B) in the Moral condition were significant.

Taken together, in the LPP late time interval there was a significant positive relationship between Moral alpha power and reaction times and a significant negative relationship with subjectively perceived emotional distress.

6. *Delta/theta ITC is related to subjectively perceived emotional distress*

A significant relationship between intertrial coherence (ITC) and subjectively perceived emotional distress scores was found only in the Moral condition.

The ITC values were from stimulus onset to 100ms, between 3-5Hz. A one-tailed bootstrapped correlation ($r = 0.439$, $p < 0.007$) was significant with a positive correlation only in the Moral condition (Fig 7C).

In sum, Moral ITC in the delta/theta bands has a significant positive correlation with participants perceived emotional distress related to the scenarios.

3. Discussion

In the present study, we investigated interindividual differences in Individualized Moral decision-making at both the behavioral and neural level. Following our three specific aims, we here report two main findings. First, our results demonstrate a central role for alpha ERSP and delta/theta phase locking – ITC and PLV - in mediating interindividual differences in Moral decision-making. Second, LPP alpha power differences between Individualized and Shared stimuli, and delta/theta ITC, all in the Moral condition, are closely related to reaction time and subjectively perceived emotional distress.

Together, our data demonstrates two main points. Firstly, interindividual differences in Moral decision-making are mediated neuronally by various markers – LPP alpha ERSP, and delta/theta ITC. Secondly, these differences are also mediated by psychological markers such as reaction time and subjectively perceived emotional distress. Our data show, for the first time, how and according to which neuronal and behavioral measures interindividual differences in Moral dilemmas can be measured.

1. Interindividual differences - Late Positive Potential (LPP) and alpha power

Our results show significant differences in alpha power between Individualized stimuli near the threshold compared to Shared stimuli far from the threshold, but only in the Moral condition. As we show (Fig 4), though alpha activity is lower in shared stimuli at an earlier time point (550ms), this decrease in alpha lasts longer in individualized stimuli as is seen between 1000 and 1600ms.

Consistent with the literature (Ferrari et al., 2008; Hajcak et al., 2009; Weinberg et al., 2012), the results show that the LPP was sensitive to affective stimuli (Brown et al., 2012; Liu et al., 2012; Hajcak et al., 2013; Minnix et al., 2013; Moran et al., 2013; Babkirk et al., 2015; Burkhouse et al., 2015) as seen in interindividual differences in perceived emotional distress (Fig 7C). These interindividual differences were evident in alpha power, as it was linked to both behavioral measures – reaction time (Fig 7A) – and subjectively perceived emotional distress (Fig 7B). Despite there being, to our knowledge, only one study which investigates alpha in a Moral context (Petras et al., 2016), it found that alpha power was significantly lower in the Moral condition compared to the non-Moral condition.

Alpha power is influenced by attention and arousal (Shaw, 1996; Cantero et al., 1999; Keil et al., 2001; Simons et al., 2003). The interindividual nature of late alpha power seen in our data (Fig 7A, B) may be through an elicited difference of attention. Self and attention have been shown to be related (Sui et al., 2013) so perhaps the drive to recruit attention is highly individual in the Moral context (Van Nunspeet et al., 2014), and the decrease in alpha seen here is related to gating (Jensen et al., 2010).

Alpha has been shown to act as a gating mechanism in sensory coding for visual stimuli (Zumer et al., 2014), and for gating inhibition generally (Jensen et al., 2010; Klimesch, 2012). These previous studies, along with our findings, show that alpha power acts to gate activity in the individual related to Moral stimuli. Our results connect individualized LPP activity and inhibition through alpha power to behavioral and subjective emotional assessments. This link shows the behavioral relevance of these neuronal measures, which can illustrate differences between individuals.

2. *Delta/theta phase-based mechanism and subjectively perceived emotional distress*

Significant differences related to stimulus proximity in delta/theta intertrial coherence (ITC) was found only in the Moral condition (Fig 5). The difference in ITC showed that participants who had higher coherence in the near proximity in the Moral condition were more distressed when reading the scenarios than those that showed no difference (Fig 7C). Since ITC measures phase consistency across trials, participants that were more consistent in phase coherence had more perceived distressed at the scenarios. The early emergence of this difference in ITC, before 200ms (Fig 6A), is consistent with the findings of implicit emotional assessments (Knyazev et al., 2009).

To build on this phase consistency measure, PLV measures synchrony between channels using phase, which here centered on Pz. In PLV, a significant difference between Moral and Control was seen for the whole epoch in the theta band (Fig 6B). The increased coherence in delta/theta relates to decision-making and memory (Jensen and Tesche, 2002; Jacobs et al., 2006; Nacher et al., 2013), attention (Digiacomo et al., 2008), and increases in theta spectral power associated with emotional visual stimuli (Güntekin and Basar, 2007; Başar et al., 2008; Güntekin and Başar, 2009; Knyazev et al., 2009).

ITC phase-related interindividual differences emerge quickly and are brief, in contrast to the longer duration of that seen in the alpha results. This was shown by the significant correlation between early ITC and subjectively perceived emotional distress (Fig 7C), which suggests that phase alignment to the stimulus is highly individual. This correlation linked this neuronal measure to a behavioral one, thus supporting its behavioral relevance.

To build on the inhibition of alpha power, event-related theta phase activity has been connected to emotional visual stimuli and emotional performance (Csukly et al., 2014). It has previously been shown that phase-related neural synchrony is involved in information processing, as is alpha power (Makeig et al., 2004). For the first time, it is shown that phase is modulated by Moral dilemmas. The results stated here isolate those changes to the delta/theta frequency range and the early part of the epoch, in the case of ITC.

Therefore, phase alignment in the early part of the epoch relates to Moral reasoning and interindividual perceived emotional distress related to the Moral dilemmas.

3. Limitations

There are several limitations to this study. To begin with, there was no direct assessment of emotion or emotional valence related to the Moral scenarios. The subjectively perceived emotional distress scores were self-reported questions done after the EEG session which asked how distressing the participant found each scenario. Many studies have examined Moral dilemmas (Strohminger et al., 2011; Manfrinati et al., 2013; Gui et al., 2015; Han et al., 2016; Pletti et al., 2016; Cellini et al., 2017) and the LPP (Brown et al., 2012; Liu et al., 2012; Hajcak et al., 2013; Minnix et al., 2013; Moran et al., 2013; Babkirk et al., 2015; Burkhouse et al., 2015) related to emotion previously. Our intention was not to replicate emotion-related results but rather look at the difference between participants on how they perceived their emotional distress related to interindividual differences at the neuronal level.

A second limitation is a lack of Control for threshold proximity. The two individualized stimuli were also the ones near the threshold. Due to the design of the study, and the aim to individualize half the stimuli to each participant, it was not possible to have two stimuli that were near the threshold but shared by all participants. The threshold itself was individualized.

The next limitation relates to the duration of the stimulus. The stimuli were presented for 2 seconds. This was short enough to prevent mind-wandering and the counting of people in the stimulus, but long enough to perceive the ratio of people killed to saved. When analysing the data, it was not possible to get reliable data for the lower frequencies (low delta) since there were less than two cycles for frequencies below 1Hz. For the PLV analysis specifically, having longer stimulus presentation would have allowed for more cycles of lower frequencies to be measured. Therefore, differences in these low frequency ranges would have been more apparent with longer stimulus duration.

Finally, the low number of scenarios presented compared to the high repetition of stimuli is the final limitation. Since the study was event-related, and we aimed to measure difference in ERP's, ERSP's and ITC related to these stimuli, many trials were needed. Though this may have led to habituation to the stimuli, there were still measurable differences related to condition.

In addition to this, to maximize consistency between scenarios – consistency of scenario structure and its components – only three scenarios were presented across the whole study. This was done to minimize the risk of introducing any confounding factors by additional scenarios. Specifically, if we used many scenarios with small differences between them, the participants' neural activity when presented with them could be different; significant aspects of the data could be lost when all trials were averaged over all scenarios. To minimize this, only scenarios which were Footbridge-type dilemmas with somewhat ecological validity, which could have the numbers of people involved made ambiguous and had a similar structure of dilemma and resulting action, were chosen from previously published studies. After employing the resulting scenarios in a pilot study, only the included scenarios were deemed ecologically valid by the pilot participants.

4. Conclusions

We investigated interindividual differences in individualized Moral decision-making at both the behavioral and neural level. It was shown that there is a central role for alpha ERSP and delta/theta phase locking in mediating interindividual differences in Moral decision-making. Finally, LPP alpha power, and delta/theta ITC are closely related to reaction time and subjectively perceived emotional distress in the Moral condition.

Taken together, our data demonstrates that interindividual differences in Moral decision-making are mediated neuronally by various markers – LPP alpha ERSP, and delta/theta ITC - as well as psychologically by reaction time and subjectively perceived emotional distress. The alpha power individual differences related to Moral reasoning arise late in the epoch, mostly after 1000ms. Phase differences related to Moral reasoning and interindividual perceived emotional distress, on the other hand, arise in the early part of the epoch.

4. Methods

1. Participants

Forty-one participants (mean age 30.59 years, range from 18 to 55 years; twenty-one female) completed all aspects of this study. The experimental protocols were approved by the research ethics committee of the University of Ottawa Institute of Mental Health Research (REB # 2009018), and the study was carried out with their permission. Written informed consent was obtained from each participant prior to study participation. In addition, all aspects of the experiment were performed according to the relevant guidelines and regulations of the University of Ottawa and its associated research institute.

All participants completed the Edinburgh Handedness Tool to determine handedness (Oldfield, 1971), the Depression Anxiety and Stress Scale 42 (DASS-42) (Lovibond and Lovibond, 1995) to rule out symptoms of depression and anxiety, and the Triarchic Psychopathy Measure (TriPM) (Patrick et al., 2009) to rule out psychopathic personality traits which have been shown to influence Moral decision-making (Blair, 1995; Blair et al., 1995; Aharoni et al., 2011; Koenigs et al., 2012). Inclusion criteria was the following: age between eighteen and fifty-five; right-handed as per the Edinburgh Handedness Tool (Oldfield, 1971); a Body-Mass Index between 18.0 and 30.0 (Olde Dubbelink et al., 2008; Babiloni et al., 2011; Del Percio et al., 2013); perfect or corrected-to-perfect vision.

The data from three participants was omitted from analysis due to TriPM and DASS-42 Scores that were outside the acceptable range (see Sup Mats). Finally, all participants were required to give a urine sample for a drug test using the Integrated E-Z Split Key Cup 5. This test screened participants for cocaine, methamphetamine, amphetamine, marijuana, and opiates. Two participants tested positive for marijuana; their data was removed from the study and not analyzed. In addition, the data from two participants were of poor quality due to technical issues during the recording session. Their data was excluded from all subsequent analysis. Therefore, the analyzed data that follows is from thirty-four participants.

2. *Behavioral Session Part 1: Varying the degree of consequentialism*

Prior to the EEG session, one behavioral session was completed by each participant to determine their behavioral consequentialist threshold (Fig 1A, Sup Fig 1). This behavioral threshold is the maximum ratio of people killed to people saved in the scenario to which each participant assented at least 80% of the time. Determining the individual threshold of each participant allowed the individualization of these stimuli for the EEG session.

Participants were presented with a Footbridge-type scenario in paragraph form (Fig 1B, Sup Table 1). Only Footbridge-type scenarios were chosen for the following reasons: they have been shown to increase relative brain activity in areas associated with emotional processing (Greene, 2001; Greene et al., 2004) and have elicited higher self-reported emotional intensities (Pletti et al., 2016) when compared to the Trolley dilemma. Since previous studies have shown that emotion is involved in decision-making of consequential Moral dilemmas (Strohminger et al., 2011; Manfrinati et al., 2013; Pletti et al., 2016), and our aim was to examine the interindividual thresholds related to these Moral dilemmas, the Footbridge scenario was used exclusively as varying the numbers of killed to saved was possible as a way of varying the consequences of the action taken.

The scenarios presented were adapted from previous studies (Greene, 2001; Sarlo et al., 2014). Specifically, the adjustment was to generalize the number of bystanders and victims in each Moral dilemma. The purpose of the behavioral session was to determine the maximum acceptable ratio of people killed to people saved in the scenario for each participant. Since we were varying the number of bystanders sacrificed and the number of victims saved, the text was changed from specific numbers to ‘several’, ‘some’, and so on. This was the focus in this study, so it was important that the numbers involved remain ambiguous. Also, our study required event-related analysis; many trials were required for ERP, ERSP and ITC analysis. To decrease the variability of neural activity between scenarios, only a small number of scenarios (two in the EEG session) were presented to maintain a consistent scenario structure, allow for ambiguous numbers of people, and maintain some believability of the scenario.

The stimuli presented during the behavioral and EEG sessions were composed of twelve two-dimensional stick-people on the left and right side of the screen, with a white line and a fixation cross down the middle separating both sides (Fig 1). As stated in the instructions, the number of people on the left side of the screen represent the number of people that are killed in the scenario presented, and the number on the right side denote the number of people that are saved in the scenario, because of the others dying.

The task of the participant was to decide whether the ratio presented was acceptable to them. For example, when presented with two people on the left side of the screen and ten on the right side, the participant must decide if killing two people - in the scenario that they had just finished reading - to save ten people is acceptable to them. Each stimulus was presented for 2 seconds. Their response took the form of either a YES or NO, with the left and right arrow key being counterbalanced across participants as to which constituted a YES response.

The behavioral session was comprised of 110 randomly ordered trials: 10 repetitions of each stimulus. All stimuli included twelve two-dimensional people, divided between the right and left side of the screen. Also, to maintain consistency, the inverse ratios were flipped images of each other. For example, the stimulus of 5:7 was the flipped image of the stimulus of 7:5, and so on. For the 6:6 stimulus, half of the trials had the original image, the other half had its flipped image.

Between the presentation of each stimulus, a fixation cross was presented (Fig 1B). This fixation cross, or intertrial interval (ITI), had a jittered duration of 5000ms, 5500ms or 6000ms, with equal numbers of the three durations in each block. The minimum duration of the ITI was calculated based on reaction times of the pilot study (see Sup Mats for details).

3. *Behavioral Session Part 2: Detection of individual threshold*

From the responses of the behavioral session, the consequentialist threshold of each participant was determined. To calculate this, two psychometric sigmoid functions were fit to the behavioral session data, one to the YES responses and one to the NO responses. These best-fit functions were calculated using the *glmfit* function in MATLAB. The point at which these two functions cross was determined to be their threshold (Fig 1A-3, Sup Fig 1) (see Sup Mats for details on the validation method).

The distribution of thresholds showed variability across participants (Fig 2A), with the distribution negatively skewed towards the more consequential thresholds. The largest group had the most consequential threshold (the difference between people saved and killed was small, while less consequential in this instance would be that the differences would be large), 5:7, though the numbers were roughly even in the other, less consequentialist thresholds.

This is consistent with previous studies, though these studies have looked at the effect of intoxication (Duke and Bègue, 2015), psychopathy (Aharoni et al., 2011; Koenigs et al., 2012), or personal versus impersonal scenarios (Wang et al., 2014) on level of consequential responses.

4. EEG Acquisition

EEG recordings were made using a 64-channel Quik-Cap (Compumedics, Charlotte, NC, USA) and were completed between 10:00am and 6:00pm. The channels on the Quik-Cap included: Fp1, Fpz, Fp2, Af3, Af4, F7, F5, F3, F1, Fz, F2, F4, F6, F8, FT7, FC5, FC3, FC1, FCz, FC2, FC4, FC6, FT8, T7, C5, C3, C1, Cz, C2, C4, C6, T8, TP7, CP5, CP3, CP1, CPz, CP2, CP4, CP6, TP8, P7, P5, P3, P1, Pz, P2, P4, P6, P8, PO7, PO3, POz, PO4, PO8, O1, Oz, O2. Additional channels were added for offline referencing, Independent Component Analysis (ICA) decomposition, and additional data: right and left mastoids, vertical ocular (above and below the left eye), and horizontal ocular (the outer canthi of the right and left eyes). The impedance of all channels was measured at less than 5kΩ before recording was initiated. Data was recorded at 1000Hz. During analysis, all files were re-referenced to the average of the two (left, right) mastoids in accordance with previous studies with a similar number of electrodes (Gui et al., 2015; Suchotzki et al., 2015; Cui et al., 2016; Hundrieser and Stahl, 2016; Pletti et al., 2016).

5. *EEG Session*

With the determination of their threshold, in the EEG session participants were presented with only four stimuli: two shared by all participants - Far from Threshold, 1:11 and 10:2 - and two individualized - Near Threshold (Fig 1A-4). Also, as per the method mentioned above, all participants were presented with two stimuli to which they had responded YES more than 80% of the time – 1:11 and Below Threshold – and two stimuli to which they had responded NO more than 80% of the time – Above Threshold and 10:2.

The EEG session was identical to the behavioral session, with two important differences: 1) the participant was only presented with four stimuli as per their behavioral session results mentioned above; and 2) each scenario had two blocks of 60 trials, with each stimulus repeated 15 times per block (Fig 1B). This session consisted of two scenarios (Sup Table 1); the order of scenarios was counter-balanced across participants.

For Control blocks, the same stimuli were presented, though the task was different. The participant was to judge whether there were more people on the left-hand side of the screen than the right-hand side. The same number of trials, same ITI, and same scenarios were presented before the beginning of the trials; all that differed were the instructions. In addition, there was no significant difference in duration between the Moral and the Control blocks. The order of these non-Moral cognitive Control blocks or Moral blocks was also counter-balanced across participants; participants with an odd number did the Moral then Control blocks, while those with an even number did the Control then Moral blocks.

Participants were seated in a dark, quiet room, between 55-60 cm away from the computer screen, as per their comfort. The experimental paradigm was presented to the participant using E-Prime 2.0 software (Psychology Software Tools, Inc., Sharpsburg, PA, USA). The EEG data was recorded with no high-pass, low-pass or notch filters at a sampling rate of 1000Hz and referenced online to the right mastoid (*data is available from A Wolff, the corresponding author*).

6. Event-Related Potential (ERP) Data Analysis

All EEG data preprocessing and analysis of the event-related potentials (ERPs) were completed using EEGLAB (versions 12,13) (Delorme and Makeig, 2004), which required MATLAB version 2014a or 2016a, including the use of the Optimization and Signal Processing Toolboxes. All statistical analysis (except for the ERSP and ITC) was completed using SPSS 24.

For preprocessing, data - recorded at 1000Hz - was resampled to 500 Hz in EEGLAB using MATLAB's *resample* function. The reason for this was purely practical, to reduce the size of the files for storage purposes. Since the highest frequency being investigated was 55Hz (in ERSP and ITC analysis), the decreased sampling rate was well above the Nyquist frequency (Weiergräber et al., 2016). The continuous data was then high-pass and low-pass filtered from 0.5Hz to 30Hz for ERP analysis according to previous studies (Chiu Loke et al., 2011; Yang et al., 2014b; Yoder and Decety, 2014; Cui et al., 2016; Petras et al., 2016), and from 0.5 to 55Hz for ERSP, ITC and PLV analysis in EEGLAB using FIR filtering (just below the 60Hz line noise).

The participants' data was then visually inspected, and epoched with a baseline of -200ms (approximately two alpha cycles) to stimulus onset. All artifacts, specifically blinks and saccades, were reduced using independent component analysis (ICA) and the Multiple Artifact Rejection Algorithm (MARA) (Winkler et al., 2011, 2014) of EEGLAB which standardized the artifact rejection process.

Participants all had a minimum of 12 clean trials per block, therefore 48-60 clean trials per stimulus per condition were included in the analysis. When Individualized stimuli was compared to Shared stimuli, two stimuli were grouped together (see Fig 1A-4). Therefore, the number of trials in this grouping was 96-120.

For each ERP component, the activity of one electrode was examined. The breakdown for each component was as follows: for N100, P300 and the LPP, Pz was the electrode chosen, and for the N200, Cz was chosen according to previous studies (Chen et al., 2009; Weinberg et al., 2012; Gable and Adams, 2013; Veit et al., 2013; Choi and Watanuki, 2014; Leuthold et al., 2014; Yoder and Decety, 2014; Burkhouse et al., 2015; Suchotzki et al., 2015; Hundrieser and Stahl, 2016). The electrode sites and time windows for these components were selected according to the literature (Olofsson et al., 2008; Chen et al., 2009; Weinberg and Hajcak, 2011; Gable and Adams, 2013; Veit et al., 2013; Choi and Watanuki, 2014; Burkhouse et al., 2015; Suchotzki et al., 2015) and visual inspection of the ERP grand average waveforms for both conditions and groups of stimuli.

The time intervals for each component, as measured in previous studies, was as follows: for the N100, 100-220ms (Veit et al., 2013); N200, 250-350ms (Suchotzki et al., 2015); P300, 350-450ms (Chen et al., 2009). For the Late-Positive Potential (LPP), the early phase (400-1000ms) and the late phase (1000-2000ms) was measured (Weinberg et al., 2012; Gable and Adams, 2013; Choi and Watanuki, 2014; Burkhouse et al., 2015) (Fig 3B). The maximum amplitude was measured for the N100, N200, and P300 (Chen et al., 2009; Veit et al., 2013; Suchotzki et al., 2015), while the mean amplitude was measured in the LPP due to the long time intervals and the fact that this was the measurement used in previous studies (Weinberg and Hajcak, 2011; Gable and Adams, 2013; Burkhouse et al., 2015).

To determine if there was a difference in activity related to the response, an ERP at Pz was time-locked to the response in each trial for all stimuli in Moral and Control (Sup Fig 3). A repeated measures t-test found no significant difference between the conditions, using the False Discovery Rate to account for multiple comparisons (Sup Fig 3).

7. *Event-Related Spectral Perturbation (ERSP) analysis*

For Event-Related Spectral Perturbation (ERSP) analysis, all preprocessing and epoching steps were identical to that of the ERP data, except that the data was low-pass filtered at 55Hz in EEGLAB using FIR filtering. Statistical differences between stimuli were measured for both conditions using EEGLAB's statistics and using the False Discovery Rate to account for multiple comparisons, at a significance level of 0.05 (Fig 4). A 3-cycle (window length of 0.8s) Morlet wavelet analysis (linear scale) was employed, with a Hanning tapered window and the Gaussian wavelet at 7Hz (results shown begin at 3Hz).

Differences in ERSP were investigated during one large time interval which comprised the intervals of the P300 and LPP (the results were illustrated from 400-2000ms in Fig 4 since there were no significant differences in the early part of the P300 time interval). As was the case in the ERP analysis, the ERSP was only measured at Pz since this is where the ERP findings were, and after visual inspection of the topographical maps for each condition and groups of stimuli.

To determine if there was a difference in activity related to the response, an ERSP at Pz was time-locked to the response for all stimuli in Moral and Control (Sup Fig 4). The response for each trial was the event to which the ERSP was time-locked. A repeated measures t-test found no significant difference between the conditions, using the False Discovery Rate to account for multiple comparisons (Sup Fig 4).

8. *Intertrial Coherence (ITC) analysis*

Intertrial Coherence (ITC) was calculated in EEGLAB (Delorme and Makeig, 2004) using the same data as for the ERSP analysis. The time interval of the entire epoch was measured, from stimulus onset to 2000ms (though Fig 5 only shows the first 600ms of the epoch since that was where the significant differences were measured).

Statistical differences between stimuli were measured for both conditions using EEGLAB's statistics, at a significance level of 0.05, with the False Discovery Rate to account for multiple comparisons (Fig 5).

9. *Phase-Locking Value (PLV) analysis*

PLV was calculated in Brainstorm (Tadel et al., 2011) using the same data from the ERSP and ITC analysis. Two frequency bands were measured, Delta (1-4Hz) and Theta (4-7Hz), and the time interval constituted the entire epoch, from stimulus onset to 2000ms. Since the ERSP and ITC were investigated only at electrode Pz, the PLV used Pz as the central electrode, with the phase-locking between Pz and four of its surrounding electrodes – P1, CPz, POz, and P2 – calculated. The mean of these four values, namely phase-locking between Pz and P1, Pz and CPz, Pz and P2, and Pz and POz, was calculated, and it was this mean value that was included in the statistical analysis.

10. *Post-Session Questionnaire Emotion Scores*

Once the EEG session had been completed, each participant responded to a question related to the three scenarios presented in the behavioral and EEG session. For each of the three scenarios, one question was asked relating to the participants' emotional assessment of each scenario. Participants responded on a visual-analog scale, and the mean of the three values (for the three scenarios) was calculated to have one value with which to correlate the neural data, thus reducing the number of correlations (see Sup Mats for more information).

5. Acknowledgements

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6. Author Contribution Statement

A.W. and G.N. conceived of the presented idea. A.W. carried out the pilot study and experiment. A.W. performed the data analysis with direction from G.N., J.G-P. and T.N. A.W. wrote the manuscript with support from G.N., J.G-P. and T.N. J.G-P. and T.N. verified the analytical methods. All authors discussed the results and contributed to the final manuscript.

7. Competing Interests Statement

The authors state no known financial or non-financial competing interests.

SUPPLEMENTARY MATERIALS

1. Methods:

1. *Participants*

The DASS-42 shows a high correlation with the Beck Anxiety and the Beck Depression Inventories (.81 and .74 respectively) (Brown et al., 1997). The TriPM was administered as it was designed for the general population and is self-report. It has three sub-scales - Boldness, Meanness and Disinhibition - that are considered to be a comprehensive view of the psychopathic personality (Drislane, 2008; Sellbom and Phillips, 2013; Venables et al., 2014).

Exclusion criteria was the following: history of psychiatric or neurological illness; history of head injury; current or history of substance abuse, including alcohol; history of radiation therapy to the head or neck; history of electroconvulsive therapy; TriPM Meanness and Inhibition scores greater than 15; DASS-42 scores for depression greater than 14, anxiety greater than 10, or stress greater than 19.

The purpose of the drug test was to rule out the presence of substances which would alter the EEG data (Banoczi, 2005; Blume, 2006).

2. *Behavioral Data Analysis*

Responses and reaction times were analyzed from the E-Prime 2.0 log files for each block of the experiment. This data was analyzed in either MATLAB 2014a or 2016b, and this data was transferred to SPSS 24 for statistical analysis.

3. *Behavioral Session Part 1: Varying the degree of consequentialism*

The scenario in the behavioral session and those in the EEG session (Sup Table 1) had roughly the same number of characters (451-452), and identical paragraph and sentence structures. Once the participants had completed reading the scenario at their own pace, they were given instructions for the task.

The minimum duration of the intertrial interval (ITI) was calculated from a behavioral pilot study which was completed in advance of this EEG study. Ten participants completed the behavioral session as structured here, and the mean reaction time of each participant was calculated. To determine the minimum ITI, the maximum reaction time from this pilot study was tripled. This maximum reaction time was 1.63 seconds, so tripled its duration was 4.89 seconds. The closest whole number was 5.0, so 5.0 seconds was the minimum ITI, with the other two ITI's increasing by half a second each.

4. *Behavioral Session Part 2: Detection of individual threshold*

The validation method involved determining between which two stimuli did the participant's YES response rate drop from greater than 80% to less than 80%. These two stimuli would then constitute those below and above the threshold. For example, one participant responded YES to 1:11 at a rate of 100%, 100% to 2:10, 90% to 3:9, 20% to 4:8, 5% to 5:7, and 0% to 6:6. According to this second method, the participant's threshold is between 3:9 and 4:8. The primary (sigmoid functions fit to the response data in the behavioral session) and verification methods were computed independently, and the same threshold was determined using both methods for all participants.

5. *Post-Session Questionnaire Emotion scores*

A 10cm horizontal line, on which the participant was directed to make a vertical mark to indicate where on the line their response fell, was presented for each question on which the participant was to respond. The vertical marks of each participant were scored in the following way: a value of zero was at the 5cm, or halfway point, between the two extremes. The more to the left of the zero, the more the negative score was given, with a maximum of -5.0. The same was true to the right of the zero; the maximum was +5.0, and the more to the right of the zero, the higher the score.

6. *Event-related potential (ERP) Data Analysis*

EEG data preprocessing was done using EEGLAB versions 12-13 (Delorme and Makeig, 2004) which worked with MATLAB version 2016a. For each stimulus for each participant, all trials were averaged. Near Threshold was comprised of Below Threshold and Above Threshold stimuli, and Far from Threshold were comprised of 1:11 and 10:2 stimuli.

2. Results:

1. *Behavioral data*

From the behavioral session, it was determined that the distribution of participants' threshold was the following: five participants had a maximum ratio of killing one person to save eleven (1:11); five participants had a maximum ratio of 2:10; four participants had a maximum ratio of 3:9; five had a maximum ratio of 4:8; fifteen had a maximum ratio of 5:7 (Fig 2A).

In the EEG recording sessions, the reaction times of all Moral trials were compared with the reaction times of all Control trials to determine if there was a significant effect of condition, regardless of stimulus. The distributions of all trials of both conditions were found to be non-normal (Moral - Kolmogorov-Smirnov p=.000, Control - Kolmogorov-Smirnov p=.000), so a nonparametric related-samples test was carried out.

Overall, the moral condition showed significantly slower reaction times, as did stimuli that were near the threshold, when compared to control and stimuli far from the threshold. Also, the difference in reaction times was retained when differences between the thresholds themselves was measured; the effect of condition on reaction times differed also, as is shown by a significant interaction.

2. Post-Session Questionnaire Emotion scores

The distribution of mean emotion scores had a mean of 0.153, median of 0.4042, and standard deviation of 2.3458 (Sup Mats Fig 4C). The range of scores was from -4.98 to 4.38, and the distribution was negatively moderately skewed, skewness = -0.515.

3. Event-related potentials (ERP's)

A repeated measures ANOVA was conducted to compare the main effect of condition and stimulus on either the maximum amplitude or mean activity for the specified electrode (Fig 3). Condition consisted of two levels (Moral, Control) and proximity to threshold consisted of two levels (Near, Far).

1. Early Components

In the early components, there was no significant main effect of Condition (Moral, Control) in the N100 (Wilks’ Lambda = .977, $F(1,30) = .670$, p = .420) or the N200 (Wilks’ Lambda = .971, $F(1,30) = .876$, p = .357) (Fig 3A). The N200 also had no significant effect of proximity to threshold (Near, Far), (Wilks’ Lambda = .982, $F(1,30) = .531$, p = .472) (Fig 3A).

2. Late Components

In the late components, there was no significant main effect of Condition (Moral, Control) in the P300 (Wilks' Lambda = 1.0, *F*(1,30) = .000, p = 1.000), the LPP early (Wilks' Lambda = .928, *F*(1,30) = 2.255, p = .144), or the LPP late (Wilks' Lambda = .991, *F*(1,30) = .272, p = .606) (Fig 3B). The LPP early also had no significant effect of proximity to threshold (Near, Far), (Wilks' Lambda = 1.000, *F*(1,30) = .000, p = 1.000) (Fig 3B).

4. Correlation between behavioral data and neural data

To determine if there was a significant relationship between behavioral data and neural data, one-tailed correlation with mean reaction times was done. To reduce the number of correlations overall, and to further focus on the difference related to proximity to the threshold, the value of the Far from Threshold variable was subtracted from the value of the Near Threshold variable.

Two additional steps taken to strengthen the statistical basis of these correlations was first to bootstrap each correlation (1000 samples), and second to halve the significance level from 0.05 to 0.025. Finally, only the LPP time intervals (400-2000ms) in the ERSP and the early (0-100ms) were measured for their relationship with behavioral data.

The first such analysis was between the difference values for the reaction times (Near Threshold reaction time minus Far from Threshold reaction time) and the

A. Alpha power is related to reaction times and emotion scores

The LPP late time interval had no significant correlation in alpha power with reaction times and the emotion scores in the control condition. One-tailed bootstrapped correlations between 1) alpha power difference values (Near Threshold minus Far from

Threshold) and reaction time difference values (*r* = 0.267, *p* < 0.085); and 2) alpha power difference values and the emotion scores (*r* = 0.029, *p* < 0.442) were not significant.

B. Delta/theta ITC is related to emotion scores

With the subset of ITC data illustrated in Fig 6A, one-tailed, bootstrapped correlations were done with the emotion scores. To reduce the number of correlations from two per condition to one, the ITC difference values were computed – ITC in Near Threshold minus ITC in Far from Threshold (Fig 7C). As above, results were significant at 0.025.

In the Moral condition, there was a significant correlation between these scores and the difference in ITC (Fig 11B). In the Control condition, in contrast, there was no significant correlation with a Pearson correlation value of *r* = 0.000, *p* < 0.500.

3. Discussion:

1. Behavioral Results

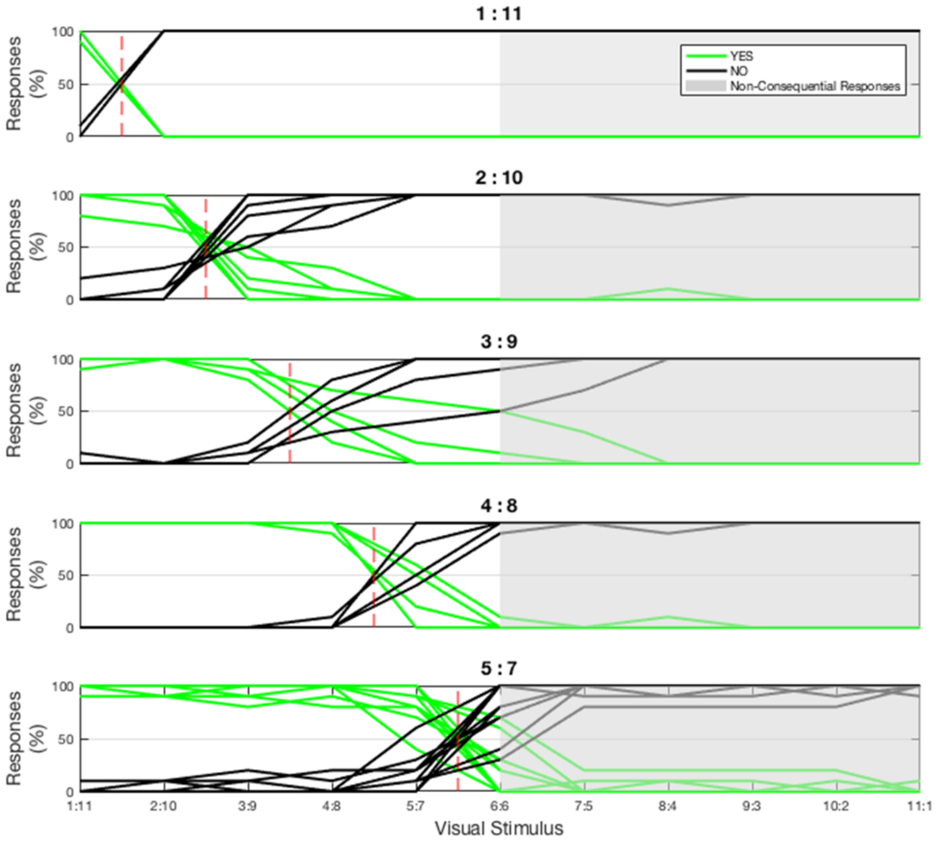
Concerning reaction times, it was determined that the Moral trials had significantly longer reaction times than Control. Previous studies have shown higher reaction times in personal dilemmas compared to impersonal dilemmas (Wang et al., 2014), and higher reaction times when family members are involved in the personal scenario compared to the involvement of strangers (Chen et al., 2009). This shows a significant effect of condition on reaction time, which can be extended to a significant effect of proximity to threshold as well. The Near Threshold stimuli had significantly longer reaction times. This indicates a more cognitively demanding task and higher conflict; this would be consistent with the results found when family members were involved in the personal dilemmas (Chen et al., 2009). The effect was maintained when the proximity to threshold was further broken down to all four stimuli as the stimuli that were above and below the threshold had higher reaction times longer than those far from the threshold, 1:11 and 10:2.

The final behavioral measure, the threshold distribution itself, had a significant effect on reaction time, with the more consequential thresholds (5:7, 4:8, 3:9) having longer reaction times than the less consequential thresholds (1:11, 2:10). Already, the effect of condition is apparent, as is the proximity to the threshold. Since our research questions concerned variability in consequentialism and inter-individual differences - both of which are measured by the varying thresholds - the behavioral results provide the foundation on which to continue with these questions when assessing our neural data.

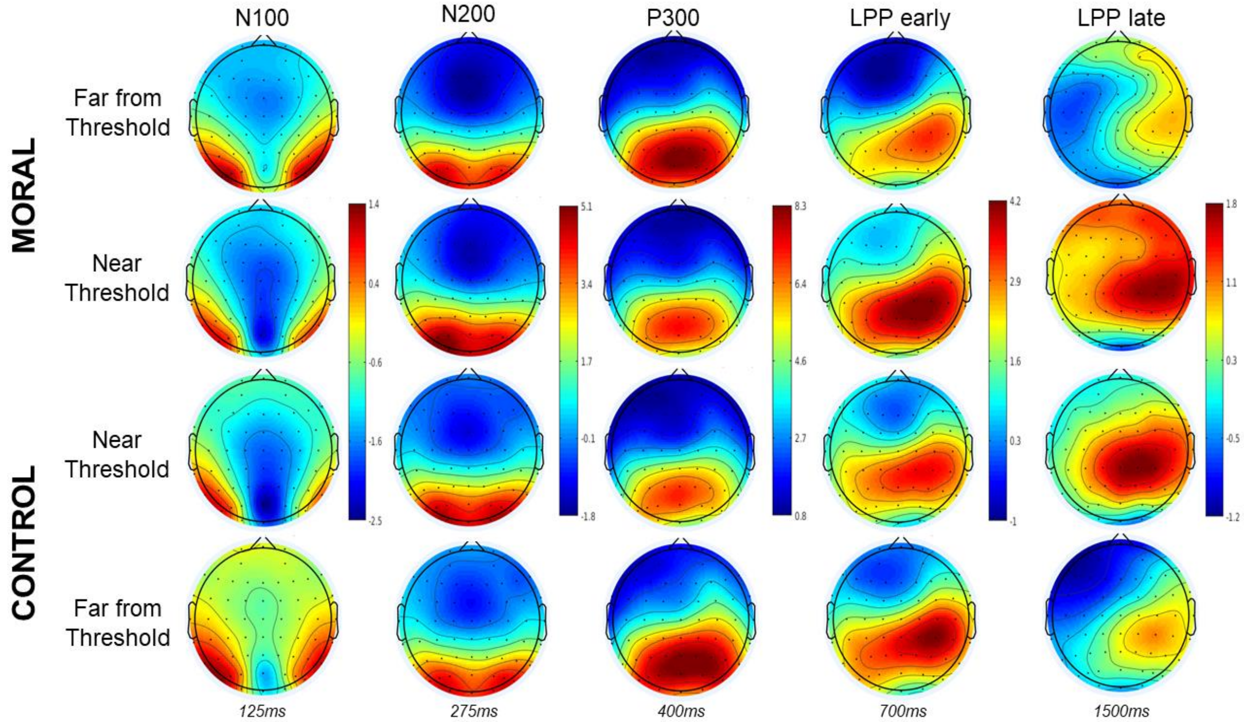
Supplementary Table 1: Study scenarios for each block. Modified from previously published studies (Greene, 2001 and Sarlo, 2014).

Block	Scenario
Behavioral Study	Like every morning, you are on your way to work and are waiting at the bus stop with some other people for the next bus to arrive. Suddenly, you realize that the bus, which is approaching at a very high speed, does not have brakes and is about to run into a group of people who are crossing the road distractedly, deep in conversation, unaware of the danger. You push the strangers next to you under the bus so that their bodies slow down the bus. You know that they will die, but the other people crossing the road will be unhurt.
EEG - Scenario 1	You are crossing a long pedestrian bridge which passes over the railway line, when you suddenly see a train moving very fast on the track below. You notice that the driver has lost control, and that the locomotive will continue its course and end up running into a group of men who are working on the adjacent tracks. On the bridge next to you are some people you do not know. You push the people off the bridge in such a way that they block the oncoming train. You know that they will die, but the group of workers will be unhurt.

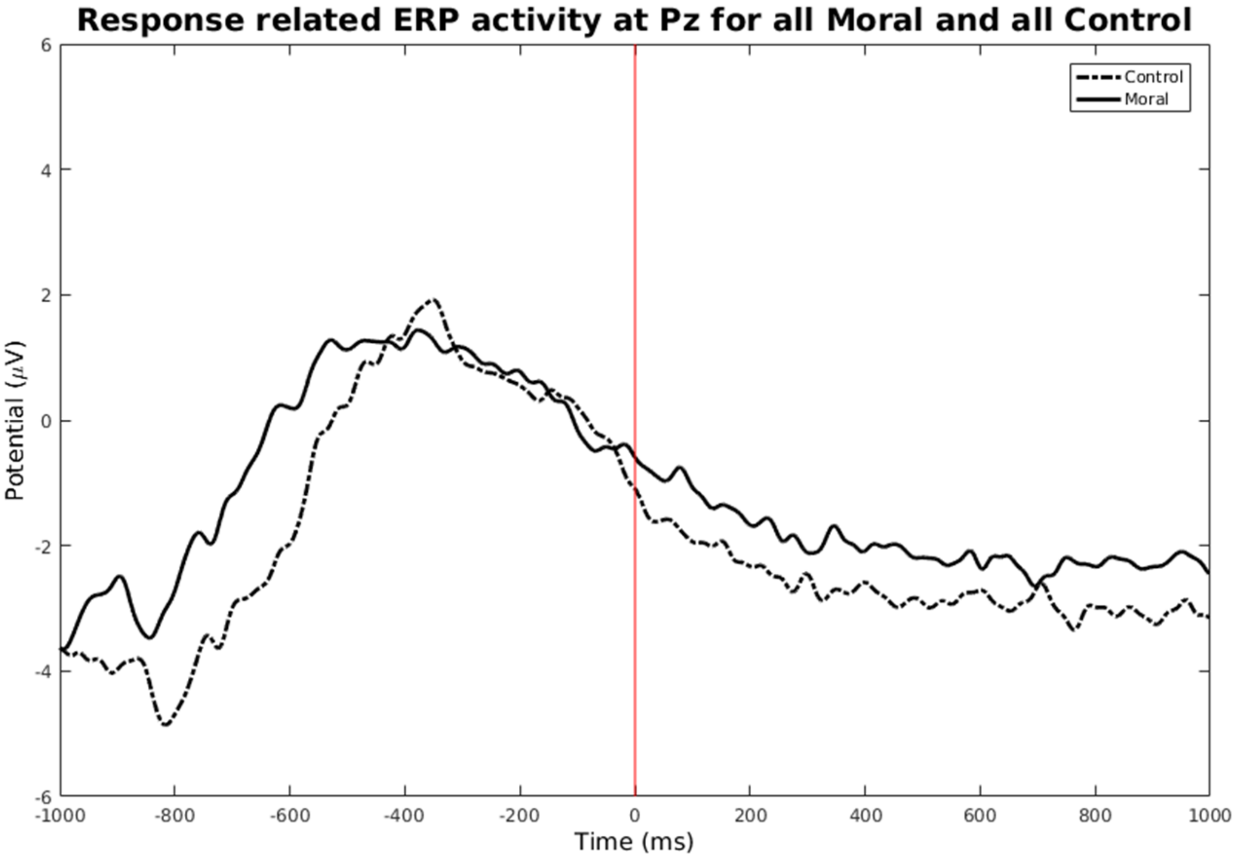
EEG - Scenario 2	You are head of a team of specialized technicians who are carrying out maintenance work on an elevator. A group of technicians are working in the elevator well, absorbed in their work. You and other technicians are on the top floor in the machine-room. Suddenly, the cable breaks and the elevator cabin starts to plummet downwards. You push some of the technicians next to you into the mechanism so that their bodies will cause the elevator to stop. You know that they will die, but the group of technicians will be saved.



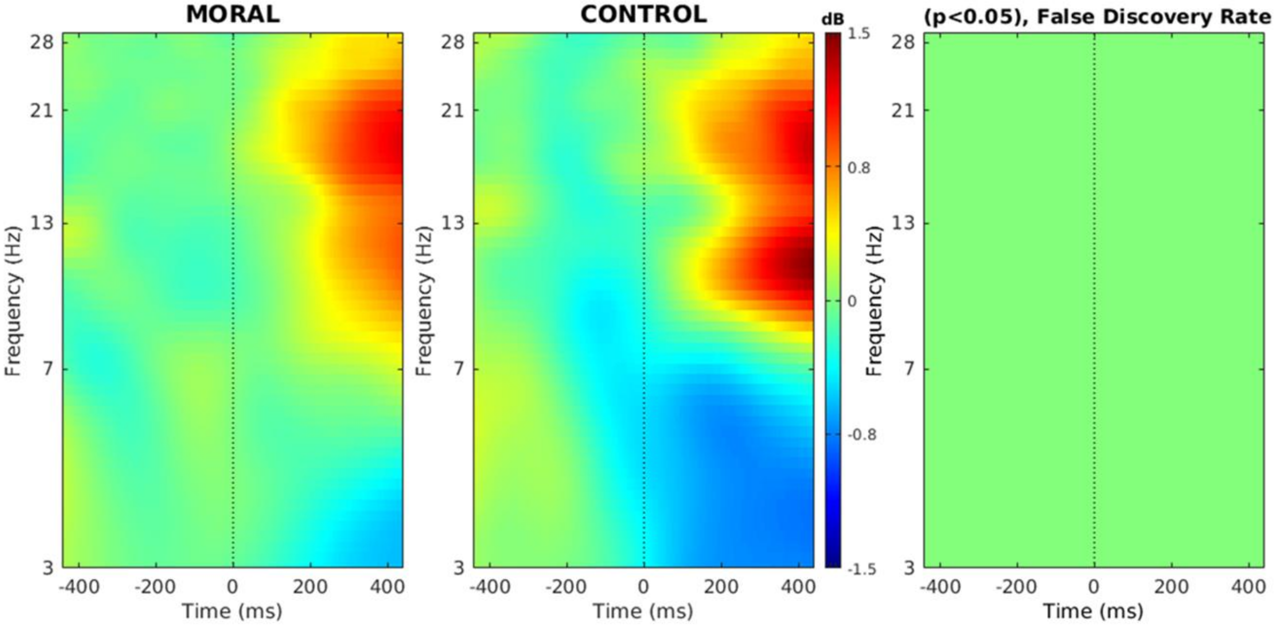
Supplementary Figure 1: YES and NO behavioral responses for all participants from the behavioral session. Each participant was given each stimulus (1:11, 2:10, 3:9, etc) ten times, in a random order. The percentage of their YES and NO responses for all stimuli were each plotted in Matlab using its *glmfit* function. The point at which the two functions crossed (illustrated above by the red dashed vertical line) was determined as the participants threshold. The stimulus just below and just above the threshold were later grouped and named Near Threshold in the EEG session. These two stimuli were thus Individualized for each participant.



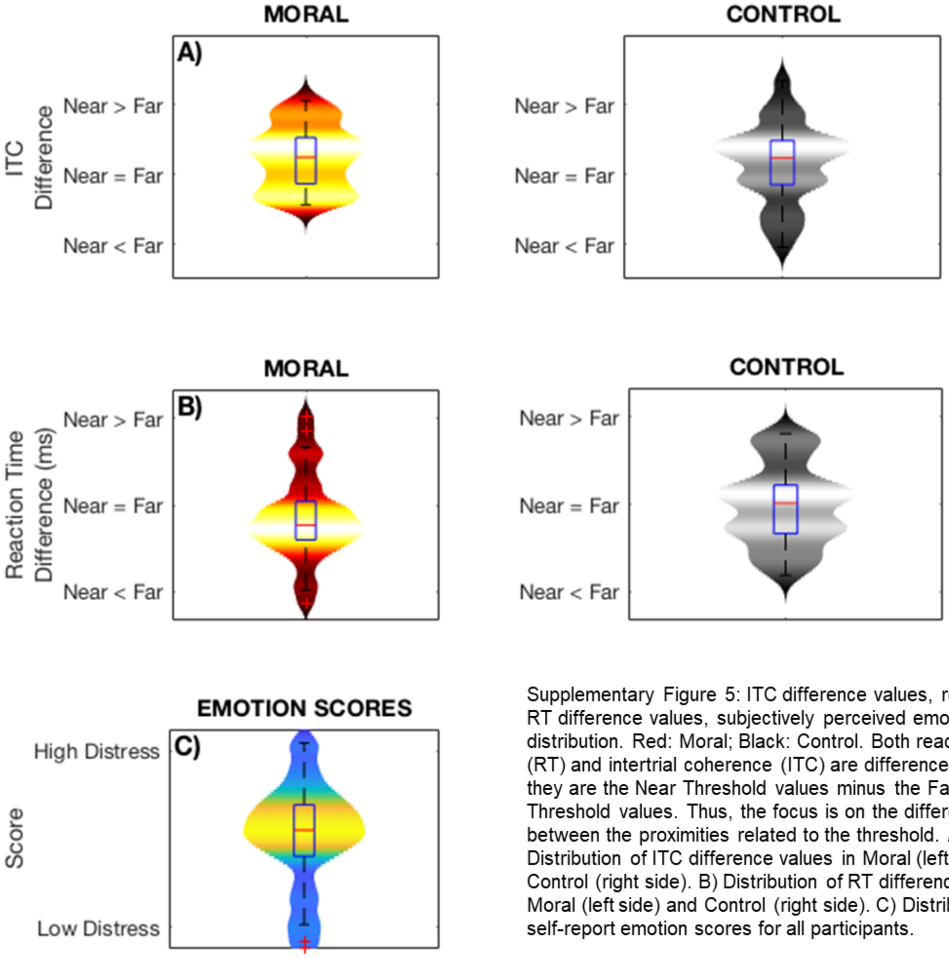
Supplementary Figure 2: Topographical maps of all four stimuli during the time interval of each component. *Rows*: stimuli, *columns*: components. The time at which each topo plot was measured is located at the bottom of each column. Colorbars are located to the right of each column.



Supplementary Figure 3: Event-related potentials (ERP's) of response at Pz for all Moral stimuli and all Control stimuli. When activity was time locked to participant responses (0ms, red vertical line), at electrode Pz there was no significant difference between all stimuli in the Moral condition and all stimuli in the Control condition. This verifies that any differences in ERP activity between conditions at Pz was not due to the response. The significance level is .05, and the t-test is corrected for multiple comparisons using the False Discovery Rate. *Solid line*: Moral, *Dashed line*: Control.



Supplementary Figure 4: ERSP of participant responses at Pz in all stimuli for Moral and Control. When activity was time locked to participant responses (0ms, black vertical dotted line), at electrode Pz there was no significant difference between all stimuli in the Moral condition and all stimuli in the Control condition. This verifies that any differences in the ERSP between conditions at Pz was not due to the response. The significance level is .05, and the t-test is corrected for multiple comparisons using the False Discovery Rate.



Supplementary Figure 5: ITC difference values, reaction time RT difference values, subjectively perceived emotion scores distribution. Red: Moral; Black: Control. Both reaction time (RT) and intertrial coherence (ITC) are difference values as they are the Near Threshold values minus the Far from Threshold values. Thus, the focus is on the difference between the proximities related to the threshold. A) Distribution of ITC difference values in Moral (left side) and Control (right side). B) Distribution of RT difference values in Moral (left side) and Control (right side). C) Distribution of self-report emotion scores for all participants.

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Article 2: Neural variability quenching during decision-making: neural individuality and its prestimulus complexity

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Conflict of Interest: No known conflict of interest.

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Abstract

The spontaneous activity of the brain interacts with stimulus-induced activity which is manifested in event-related amplitude and its trial-to-trial variability (TTV). TTV describes the variability in the amplitude of the stimulus-evoked response across trials, and it is generally observed to be reduced, or quenched. While such TTV quenching has been observed on both the cellular and regional levels, its exact behavioral relevance and neuronal basis remains unclear. Applying a novel paradigm for testing neural markers of individuality in internally-guided decision-making, we here investigated whether TTV (i) represents an individually specific response by comparing individualized vs shared stimuli; and (ii) is mediated by the complexity of prestimulus activity as measured by the Lempel-Ziv Complexity index (LZC). We observed that TTV - and other electrophysiological markers such as ERP, ERSP, and ITC – showed first significant differences between individualized and shared stimuli (while controlling for task-related effects) specifically in the alpha and beta frequency bands, and secondly that TTV in the beta band correlated significantly with reaction time and eLORETA activity. Moreover, we demonstrate that the complexity (LZC) of neuronal activity is higher in the prestimulus period while it decreases during the poststimulus period, with the former also correlating specifically with poststimulus individualized TTV in alpha (but not with shared TTV). Together, our results show that the TTV represents a marker of 'neural individualization' which, being related to internal processes on both neural and psychological levels, is mediated by the information complexity of prestimulus activity. More generally, our results inform the pre-post-stimulus dynamics of rest-stimulus interaction which is a basic and ubiquitous neural phenomenon in the brain and highly relevant for mental features including their individuality.

Introduction

General background – Variability as marker of neural and psychological individuality

Variability in brain activity between participants has long been treated as meaningless noise or measurement error (Arazi et al., 2017a; Seghier and Price, 2018). This neural variability, especially in task-evoked responses, however, has recently been shown to explain the behavioral and perceptual differences of individual participants (Haigh et al., 2015; Arazi et al., 2017b, 2017a), thus challenging this view. The finding may provide measures of specifically individual features of brain activity (Arazi et al., 2017b, 2017a), and so address an urgent desire for individualized neural markers, a growing concern in both basic and clinical neuroscience (Braver et al., 2010; Reineberg et al., 2015; Friedman and Miyake, 2016; Jang et al., 2017; Seghier and Price, 2018).

What purpose, though, does a better understanding of these interindividual differences serve? Cognitive studies often show major intra- and interindividual differences in both neuronal and behavioral responses to stimuli. Given that the stimuli or tasks are the same for all subjects, one would rather expect similar changes in neural and behavioral responses across subjects, however this is not the case. It raises the question as to the origin of this interindividual variability and its neural markers. Determining these sources of variability is even more pressing in clinical settings. Here, intersubject variability may provide explanations as to why symptoms differ between patients with similar lesions, or those with the same symptoms have different outcomes (Seghier and Price, 2018). Investigating these differences may shed light on the underlying mechanisms of these clinically significant variances.

Variability of task-evoked activity, as manifested in trial-to-trial variability quenching, has been consistently observed on multiple levels of neural activity, including cellular recordings (Arieli et al., 1996; Monier et al., 2003; Finn et al., 2007; Churchland et al., 2010, 2011; Hussar and Pasternak, 2010; Scaglione et al., 2011; Chang et al., 2012; White et al., 2012; Goris et al., 2014; Mazzucato et al., 2015, 2016; Liu et al., 2016), electroencephalography/electrocorticography (EEG/ECoG) (He and Zempel, 2013; Schurger et al., 2015; Arazi et al., 2017b, 2017a), and functional magnetic resonance imaging (He, 2013; Ferri et al., 2015; Huang et al., 2017b) (see also (Dinstein et al., 2015) for review of TTV). These data demonstrate that TTV quenching is a ubiquitous phenomenon of neural activity and is a result of a nonlinear interaction between the brain’s ongoing spontaneous activity and activity induced by the stimulus (He, 2013; Huang et al., 2017b). The exact behavioral relevance and underlying neuronal mechanisms of TTV quenching, however, remain unclear.

In humans, this quenching of activity is unchanging in the individual over time and across tasks (Arazi et al., 2017b), and is related to behavioral performance (He and Zempel, 2013; Haigh et al., 2015; Schurger et al., 2015; Arazi et al., 2017a, 2017b); stronger TTV quenching is associated with faster reaction times (He, 2013), superior perceptual abilities (Schurger et al., 2015; Arazi et al., 2017b; Baria et al., 2017), and superior memory recall (Xue et al., 2010). When taken together, these results suggest that TTV quenching is strongly related to internal - individual or self-specific - neural processing; TTV may thus be a marker of an individualized neural response.

What, however, are the sources of TTV? It has been shown that prestimulus (He, 2013) and resting state activity (Huang et al., 2017b) influence trial-to-trial variability, which suggests that TTV is partly due to internal - pre-stimulus - rather than external - stimulus-related - sources. The influence of the two – internal and external – implies that TTV is a hybrid of the impact of both internal prestimulus activity levels and external stimulus-related effects (Huang et al., 2017b). To test this hypothesis, we require an operational distinction between the effects of internal activity and those of the external stimulus on the commonly shared output, the stimulus-induced or task-evoked activity in the post-stimulus period.

The operational distinction between internal and external effects can, on a psychological level, be studied comparing internally-guided (IDM) and externally-guided decision-making (EDM) (Nakao et al., 2009, 2012, 2013a). In IDM, no correct answer based on external criteria exist; participants respond based on their own internal preferences – this reflects individuality on a psychological level (Nakao et al., 2012). In contrast, in EDM there is one correct answer based on external criteria (Nakao et al., 2012) as would be the case if given two words and asked which was longer (Nakao et al., 2009).These studies show differential neural correlates for IDM and EDM (Nakao et al. 2012, 2013, 2016); the differential impact of IDM and EDM on TTV, as well as potentially different roles of pre-stimulus activity, however, remain to be studied. We therefore combine here investigation of TTV and pre-stimulus effects in the context of IDM vs EDM to probe for the neural correlates of internal and external effects on TTV.

Main aim – Internal prestimulus origin of poststimulus trial-to-trial variability

The main aim of our study, then, was to determine if internal, pre-stimulus ongoing neural activity contributes to the source of task-evoked variability as measured with TTV. We hypothesize that TTV is a marker of neural individuality as it can originate only from the internal neural activity and, more specifically, its pre-stimulus complexity (see below). To test this hypothesis, we converged an IDM/EDM paradigm with TTV measures and analysis of pre-stimulus activity; this allowed us to study the internal and external sources of individuality with respect to TTV on both the neural and psychological levels.

A study in which participants were presented with identical stimuli - in one condition they were to make internally guided decisions while the second condition demanded externally guided decisions (Nakao et al., 2009, 2012, 2013a) – was designed to specifically investigate this question. The IDM condition employed here was a task adapted from previous studies (Sarlo et al., 2012; Manfrinati et al., 2013; Pletti et al., 2016) and cited as an example of IDM which allows to test for individuality on the psychological level of the task (Greene, 2001; Greene et al., 2004; Moll et al., 2006, 2008; Moll and de Oliveira-Souza, 2007; Greene and Paxton, 2009; Nakao et al., 2012).

To further test the specificity of TTV quenching, participants were presented with four stimuli, two individualized to them and two shared by all participants (Wolff et al., 2018), similar to the high- and low-conflict stimuli used in a past IDM/EDM study (Nakao et al., 2013a). In this 2x2 factorial design, our aim was to determine if TTV quenching was significantly different in IDM when compared to EDM, and if there was a difference – across conditions or specific to one condition – in TTV between individualized stimuli and stimuli shared by all participants. This allowed us to operationalize individuality on the psychological level with respect to both task – IDM vs EDM – and stimuli – individualized vs shared.

TTV quenching is related to event-related desynchronization which has been shown in alpha, beta and gamma (Arazi et al., 2017a). Specifically, the alpha frequency band seems to exhibit a special role for individuality as it has long been shown to be highly individual (Posthuma et al., 2001; Klimesch et al., 2007; Bröltzner et al., 2014; Gruber et al., 2014; Mierau et al., 2017) and related to self-related stimuli (Bai et al., 2016). For that reason, we investigated TTV quenching in specific frequency bands, with a specific focus on alpha as possible marker of neural individuality. That extends previous TTV investigations that have been conducted only in the broadband, not in specific frequency bands such as alpha.

Specific aims – TTV as individual neural marker and its pre-stimulus complexity

The first specific aim of our EEG study consisted in testing TTV as an individual neural marker by applying a novel study design in an IDM paradigm (Lieberman and Pfeifer, 2005; Volz et al., 2006; Nakao et al., 2012, 2016). We hypothesized that there would be significant differences in TTV quenching - specifically in alpha, beta and gamma bands previously shown to correlate with decreases in power (Arazi et al., 2017b) - as well as differences in other electrophysiological markers (ERP, ERSP, ITC) in response to individualized stimuli compared to stimuli shared by all participants.

In addition to its modulation by different stimuli (Churchland et al., 2010, 2011; Hussar and Pasternak, 2010; Arazi et al., 2017b), TTV is also dependent upon the degree of the brain's internal prestimulus variance as observed on both cellular (Kisley and Gerstein, 1999; Curto et al., 2009; Schurger et al., 2010; Pachitariu et al., 2015) and regional levels (He, 2013; Schurger et al., 2015; Huang et al., 2018). This strongly suggests that features of the prestimulus activity, such as its complexity, mediate TTV quenching.

Based on these findings, the second aim of our study was to characterize prestimulus activity in terms of its informational complexity. This was achieved by applying the well-known Lempel-Ziv complexity measure (LZC) (Lempel and Ziv, 1976) which has been used widely in EEG/MEG studies (Fernández et al., 2009, 2011, 2012; Takahashi, 2013; Ibáñez-Molina et al., 2015; Mateos et al., 2018). We hypothesized that the degree of prestimulus complexity, as measured through LZC (Mateos et al., 2018), is directly related to the degree of TTV quenching in response to individualized (rather than shared) stimuli.

Notably, to disentangle internal (prestimulus) and external (stimulus-related) effects on TTV, we introduced a novel method for TTV calculation in EEG by calculating TTV independent of the variance at stimulus onset. This would confound prestimulus effects and TTV calculation. This was accomplished by using pseudotrials - trials when a stimulus is absent (Huang et al. 2017) - to compare with actual trials and to calculate poststimulus variability through TTV (see Huang et al 2017 for an analogous method in fMRI).

Overview – From ERP, ERSP, and ITC over TTV to pre-stimulus Lempel-Ziv complexity

We recorded electroencephalography (EEG) and response activity in human subjects while they performed a visual IDM and EDM task adapted from previous studies (Sarlo et al., 2012; Manfrinati et al., 2013; Pletti et al., 2016). To individualize two of the four stimuli presented in the EEG session, a behavioural session was completed prior to it to determine the response thresholds of the participants. As done in a previous study (Arazi et al., 2017a), we started by measuring event-related potentials (ERPs) to determine that there was an effect of the stimuli on evoked activity. Next, we measured the event-related spectral perturbation (ERSP) and intertrial coherence (ITC) to establish if there were differences between stimuli or conditions in frequency band power and phase consistency, and if so, which bands.

We then measured TTV by calculating the TTV index, a new measure, which incorporates pseudotrials (Huang et al., 2017b), and investigated the effect of stimulus and condition in the broadband and individual frequency bands. In only those bands found to have significant differences, we correlated the TTV index values to the response-related measures from the EEG session (threshold, reaction time) to see if our neural measure related to the behaviour of the individual participants. Finally, we measured LZC in the internal prestimulus activity and correlated it with the TTV index values in the significant bands; this served the purpose of determining if, and for which stimulus or condition, the prestimulus complexity relates to the poststimulus effect of the external stimulus.

Methods

Participants

Thirty-four right-handed (Oldfield, 1971) participants (age: mean = 30.6 ±11.0 years, range = 18-55 years; 18 female) completed this study. All participants were free of psychiatric diagnoses or history of psychiatric illness, neurological illness or history of head injury, and had perfect or corrected-to-perfect vision. The experimental protocols were approved by the research ethics committee of the University of Ottawa Institute of Mental Health Research (REB # 2009018), and the study was carried out with their permission. Written informed consent was obtained from each participant prior to study participation.

Determining individualized stimuli

For the EEG session, two of the four stimuli presented were individualized according to a response threshold in the IDM condition. The IDM task was a consequential moral dilemma adapted from previous studies (Sarlo et al., 2012; Manfrinati et al., 2013; Pletti et al., 2016) as an example of IDM (Greene, 2001; Greene et al., 2004; Moll et al., 2006, 2008; Moll and de Oliveira-Souza, 2007; Greene and Paxton, 2009; Nakao et al., 2012).

The moral dilemma scenarios presented a situation in which participants would push some strangers to their deaths to save another group of strangers. They were adjusted from EEG studies (Sarlo et al., 2012; Manfrinati et al., 2013; Pletti et al., 2016) only to generalize the number of bystanders and victims. The purpose of this was to determine the maximum acceptable ratio of people killed to people saved in the scenario for each participant. Since we were varying the number of bystanders sacrificed and the number of victims saved, the text was changed from specific numbers to ‘several’, ‘some’, and so on.

After the participants had read the scenario at their own pace, the stimuli presented were composed of twelve two-dimensional stick-people on the left and right side of the screen, with a white line and a fixation cross down the middle separating both (Fig 1A).

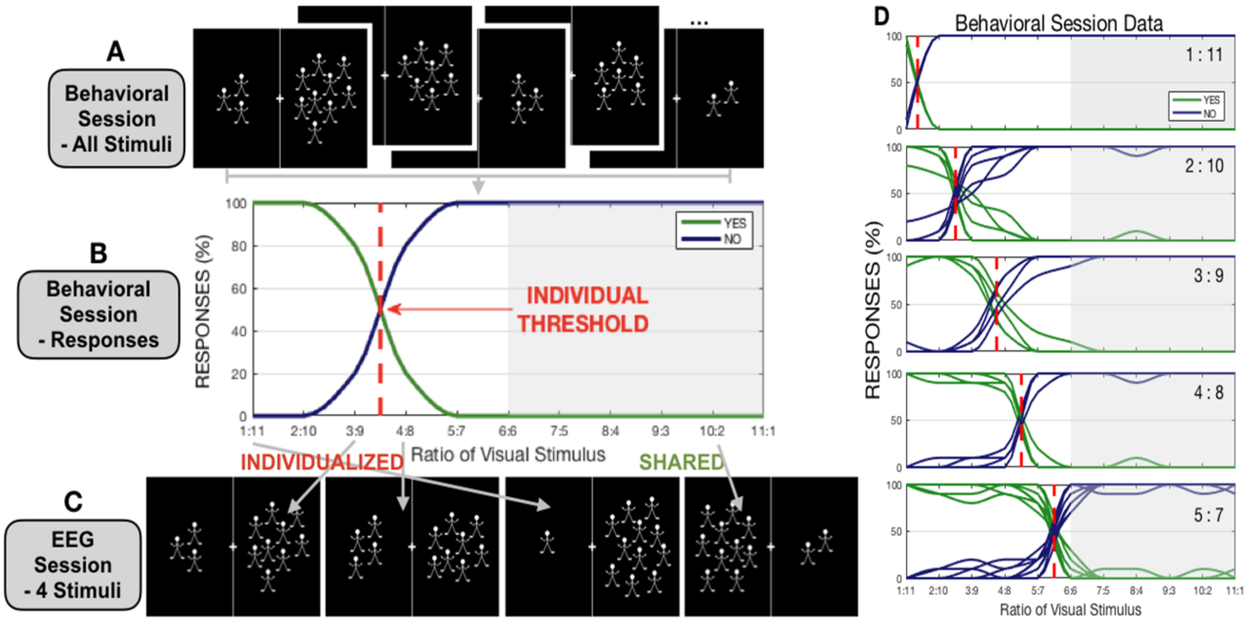


***Figure 1**: Study threshold determination and behavioral session results. **A)** Determination of threshold in behavioral session. Participants read a scenario (see Wolff et al, 2018) in the behavioral session. Participants were presented with 10 repetitions of each stimulus. **B)** Based on the percentage of YES and NO responses for each stimulus in the behavioral session, the threshold (dashed red vertical line) was calculated. **C)** The stimuli immediately below and above the threshold - the individualized stimuli - as well as two other stimuli shared by all participants - 1:11 and 10:2 - were the only stimuli presented to participants in the subsequent EEG session. **D)** Response results from the behavioral session for all participants. Thresholds were calculated in MATLAB using their glmfit function. Five participants had a threshold of 1:11, 2:10, and 4:8, while four participants had one of 3:9. The largest group was 5:7 with fifteen participants.*

The number of people on the left side represent the number of people that are killed in the scenario, and the number on the right side denote the number of people that are saved because of the others dying.

The task of the participant in this threshold determining behavioral block – as well as during the IDM task of the EEG session - was to decide whether the ratio presented was acceptable to them. Each stimulus was presented for 2 seconds and their response took the form of either a YES or NO, with the left and right arrow key being counterbalanced across participants as to which constituted a YES response. The participants were presented with 10 repetitions of each stimulus, in a random order. All stimuli included twelve two-dimensional people however the ratio between the left and right side differed. A fixation cross was presented between each stimulus as the intertrial interval with a jittered duration of 5000ms, 5500ms or 6000ms.

To calculate the response threshold of each participant, two sigmoid functions were fit, one to the YES responses and one to the NO responses using the *glmfit* function in MATLAB (Fig 1B). The point at which these two functions cross was determined to be their threshold. Therefore, the stimulus immediately below and above the threshold were the individualized stimuli presented in the EEG session while two stimuli at the extreme ends of the ratios (1:11 and 10:2, all participants responded YES and NO consistently during the behavioral session) were presented to all participants as the shared stimuli (Fig 1C). For all 34 participants, there was variability in the response threshold with each participant falling under one of five thresholds (Fig 1D).

EEG Session

EEG recordings were made using a 64-channel Quik-Cap (Compumedics, Charlotte, NC, USA). Additional channels were added for offline referencing (mastoids) and Independent Component Analysis (ICA) decomposition (vertical and horizontal ocular). The impedance of all channels was measured at less than 5kΩ before recording was initiated. During analysis, all files were re-referenced to the average of the two (left, right) mastoids.

Participants were seated in a dark, quiet room, between 55-60 cm away from the computer screen, as per their comfort. The experimental paradigm was presented using E-Prime 2.0 software (Psychology Software Tools, Inc., Sharpsburg, PA, USA). The

EEG data was recorded with no high-pass, low-pass or notch filters at a sampling rate of 1kHz and referenced online to the right mastoid.

The EEG session was identical to the behavioral session, with two important differences: 1) the participant was only presented with four stimuli (two shared by all participants and two individualized (Fig 1C)), and 2) each scenario had two blocks of 60 trials, with each stimulus repeated 15 times per block. All participants were presented with two stimuli to which they had responded YES more than 80% of the time – 1:11 and just below threshold – and two stimuli to which they had responded NO more than 80% of the time – above the threshold and 10:2. The order of scenarios was counter-balanced across participants.

For EDM blocks, the same stimuli were presented, though the task was different as is consistent with previous IDM/EDM paradigms (Nakao et al., 2009, 2013b). The participant was asked whether there were more people on the left side of the screen than the right side. The same number of trials, same ITI, and same scenarios were presented before the beginning of the trials. The order of the IDM or EDM blocks was counter-balanced across participants.

EEG preprocessing

All EEG data preprocessing was completed using EEGLAB (v12, v13) (Delorme and Makeig, 2004), which required MATLAB (The MathWorks) v2018a, including the use of the Optimization, Statistics and Signal Processing Toolboxes. All statistical analysis (except for the event-related spectral perturbation and intertrial coherence measures) was completed using SPSS v24 (IBM).

Data was resampled to 500 Hz using EEGLAB's *resample* function. The continuous data was then low- and high-pass filtered (FIR filter) from 0.5Hz to 70Hz, and a notch filter applied at 60Hz to eliminate electrical line noise.

The data was then visually inspected. If channels were flat longer than 5s, had less than .80 correlation with neighboring channels, or had line noise greater than 4 standard deviations difference compared to other channels, they were removed. The mode of channels removed for all participants were 2, with the range being 0 to 5.

The continuous data was then epoched with a baseline of -200ms to stimulus onset. All files were referenced to the average of the two mastoids. All stationary artifacts, specifically eye movements, were reduced using Independent Component Analysis (ICA) and the Multiple Artifact Rejection Algorithm (Winkler et al., 2011, 2014).

Event-related potential, event-related spectral perturbation and intertrial coherence analysis

To begin, we measured two event-related potential (ERP) components to establish the effect of stimulus and condition: the N100 and the P300. Both components were measured at electrode Pz which was determined according to previous literature (Chen et al., 2009; Veit et al., 2013; Wang et al., 2014; Cui et al., 2016; Gan et al., 2016) and visual inspection of the ERP grand average waveforms for both conditions and groups of stimuli. The peak amplitude of each component was measured in a 2x2 (condition, stimulus) repeated measures ANOVA from time intervals taken from previous studies (Chen et al., 2009; Veit et al., 2013): 100-220ms for the N100, 350-450ms for the P300.

After finding a significant effect of stimulus in the ERP analysis, event-related spectral perturbation (ERSP) and intertrial coherence (ITC) was measured from stimulus onset to 450ms (end of P300 interval) at the same electrode. This was done to determine if there was a difference in frequency band power and phase coherence between conditions or stimuli, and if so, in which bands.

A three-cycle Morlet Wavelet analysis was employed in EEGLAB, with a Hanning tapered window. For these two measures, statistical differences were calculated in EEGLAB with a paired sample *t*-test using its statistics (significance level of .05) and applying the False Discovery Rate (Benjamini and Hochberg, 1995) to account for multiple comparisons.

To determine if there was a difference in activity related to the response, an ERP and ERSP at Pz was time-locked to the response in each trial. A repeated measures *t*-test found no significant difference between the conditions or stimuli.

For ITC, the coherence for each stimulus in each condition was extracted between 0 and 100ms and between 3.92-6.13Hz (the nearest data points between 4 and 6Hz) to measure correlations with ERP peak amplitudes (Fig 3B, C). The data was extracted from 0-100ms due to the significant results found in the ITC analysis in Figure 3B.

Trial-to-trial Variability index calculation

Next, we measured trial-to-trial variability (TTV) to investigate the quenching of neural activity after stimulus onset. In this study, TTV was measured as the variability changes with respect to stimulus onset (see (He and Zempel, 2013; Arazi et al., 2017a, 2017b) for related methods). This method allowed for the calculation of a time-resolved TTV;

each poststimulus timepoint measured variability relative to stimulus onset. In addition, to separate effects in the trial-to-trial variability (TTV) related to the stimulus from the effects of ongoing variability, the use of pseudo trials (Huang et al., 2017b), trials without a stimulus (Dinstein et al., 2015), were used.

Pseudo trials were calculated from the intertrial intervals (ITIs) in which a virtual stimulus was inserted (Fig 4A). ITIs were jittered to be 5s, 5.5s and 6s while the stimulus duration was 2s, so pseudo trials were inserted during this ITI period. The actual trials – and therefore the pseudo trials – were extracted from 500ms prior to stimulus onset until 2s after stimulus onset. For a 5s ITI, the pseudo stimulus onset was inserted 3.5s prior to the actual stimulus onset. Before this, a 1s buffer between the actual trial and the pseudo trial was taken to allow for any activity related to the fixation cross onset to return to baseline. In the 5.5s and 6s ITIs, the buffer between the pseudo trial and the actual trial increased from 1s in the shortest ITI to 1.5s and 2s in the longest.

Though neural activity was only analyzed from stimulus onset to 450ms, the duration of the stimulus continued to 2000ms. From the inserted pseudo trials, TTV of the pseudo stimulus was calculated in the same way as the actual stimulus (Fig 4A) (see Huang et al, 2017 for a similar method in fMRI).

To account for the change in variability related to the stimulus itself, the pseudo trial TTV was subtracted from the actual trial TTV from 200 to 800ms post stimulus for each timepoint (Fig 4B). This was done to account for the ongoing spontaneous fluctuations of the neural activity, therefore correcting for this in the calculation of the TTV. The mean was then calculated, yielding one value, the TTV index.

Cognitive tasks are known to have differential effects on frequency bands (Klimesch, 1999, 2011, 2012; Jokisch and Jensen, 2007; Jensen et al., 2010, 2014; Klimesch et al., 2011; Fellinger et al., 2011; Buzsáki and Silva, 2012; Buzsáki and Wang, 2012; Zumer et al., 2014; Bonnefond and Jensen, 2015). For this reason, and the significant differences found in the ERSP (Fig 3A) and ITC (Fig 3B), the continuous EEG data was filtered into frequency bands before being epoched according to above methods. The frequency ranges were as follows: broadband was 0.5-70Hz; theta was 4-8Hz; alpha was 8-13Hz; beta was 13-30Hz; gamma was 30-70Hz. The TTV index was calculated in these filtered bands in the same way as the broadband (Fig 5, Sup Mats).

To determine if there was an effect of condition or stimulus in each band, a 2x2 (condition, stimulus) repeated measures ANOVA was calculated for each band. All *p*-values were False Discovery Rate (Benjamini and Hochberg, 1995) corrected for multiple comparisons.

Effect of Threshold on TTV index

After finding significant differences in the TTV index for specific frequency bands, we sought to relate these neural measures to our behavioral data. To start, we tested whether the threshold had a significant effect on the TTV index. Participants were grouped into three groups (low, middle, high) according to their threshold only in the TTV index bands found to be significant in the above analysis. This was done to ensure that roughly an equal number of participants were in each group (low = 10 participants, middle = 9 participants, high = 15 participants).

To determine if threshold had an effect - or interaction - with either factor in the significant TTV index bands, a 2x2x3 (condition, stimulus, threshold) repeated measures ANOVA, with a between subjects' factor of threshold, was done on the absolute value of the TTV index.

Reaction time correlations with TTV index

Next, to determine if the mean reaction times correlated with the TTV index in either of the significant bands, we performed one-tailed, bootstrapped (1000 samples) Pearson correlations with significance at .05. Since our experimental design focused on the difference between the individualized and shared stimuli, we first calculated the differences between them for each measure; the TTV indices and mean reaction times shared values were subtracted from the individualized value. This was done to emphasize the difference between them.

Lempel-Ziv Complexity analysis

As one of our aims was to determine if prestimulus activity related to our poststimulus TTV index measure, we applied a measure of complexity from information theory (Gershenson and Fernandez, 2012) to the non-baseline corrected data. Lempel-Ziv Complexity (LZC) was calculated based on previous studies (Aboy et al., 2006; Casali et al., 2013) in MATLAB v2018a using a custom script. In both the pre- and poststimulus periods for which LZC was calculated, 500ms of the signal was measured.

To calculate LZC, the EEG signal was first converted into a binary sequence. For each data point in a timeseries $x(i)$, a symbol sequence $s(i)$ is calculated:

$$s(i) = \begin{cases} 0 & if\ x(i) < T_d \\ 1 & if\ x(i) \geq T_d \end{cases}$$

where T_d is the threshold (Aboy et al., 2006). In the complexity equation used here, the threshold was the median. This binary sequence $s(i)$ is then scanned from left to right and the complexity measure $c(n)$ is increased by one each time a new sequence of consecutive values occurs (Aboy et al., 2006). Finally, the complexity value $C(n)$ is normalized to control for signal length as follows:

$$C(n) = \frac{c(n)}{\frac{n}{\log_2(n)}}$$

where n is the length of the $c(n)$ sequence.

We first determined if there was a difference between the pre- and poststimulus LZC in all stimuli (Fig 7A), the difference between these two values was calculated, and the difference between stimuli in each condition was measured (Fig 7B). Paired-sample bootstrapped (1000 samples) *t*-tests were done for each of these tests, with the False Discovery Rate (Benjamini and Hochberg, 1995) correction applied to all *p*-values.

Finally, to determine if there was a relationship between prestimulus activity, as measured by LZC, and the TTV indices from the significant bands, one-tailed bootstrapped (1000 samples) Pearson correlations were conducted (Fig 8), with the False Discovery Rate (Benjamini and Hochberg, 1995) applied to each correlation.

eLORETA source localization

To support our findings, we investigated whether activity in the visual cortex (due to the visual paradigm) also has a relationship with the TTV index in the significant bands. To answer this, we performed source localization using eLORETA (Pascual-Marqui, 2007) on the software of the KEY Institute at the University of Zurich (Pascual-Marqui et al., 1994). We chose one region of interest (ROI), the primary and secondary visual cortices (BA 17 and 18) and calculated the mean activity in this ROI from stimulus onset to 200ms, the beginning of the TTV index calculation. Bootstrapped (1000 samples) one-tailed Pearson correlations between this activity and the TTV indices were performed for both stimuli and conditions, with the False Discovery Rate correction (Benjamini and Hochberg, 1995) was applied to all *p*-values to correct for multiple comparisons.

After the correlations with our main ROI, we performed a second group of correlations with three control regions. This was done to determine if our findings were specific to the visual cortices. We chose the premotor cortex (BA 6) first as it has not shown to be active during IDM tasks (Han et al., 2016) and was expected to show no difference between conditions or stimuli. The other two control regions, the posterior cingulate cortex (BA 29/30, 23/31) (PCC) and inferior parietal lobules (BA 39, 40) (IPL) are part of the default mode network and have been shown to be active during IDM tasks (Han et al., 2016; Boccia et al., 2017). If we found significant correlations in these two regions then the effect would not be specific to the visual cortices, but rather consistent across regions known to show activation during IDM tasks.

The same correlations were performed and the False Discovery Rate correction (Benjamini and Hochberg, 1995) was applied to all *p*-values.

Results

Threshold determination

The threshold of each participant was determined in the behavioral session prior to EEG recording. It was calculated in MATLAB from two sigmoid functions fit to the YES and NO responses of each participant. The point at which the two functions crossed was determined to be the threshold (Fig 1B, D).

Variability across participants was shown by the resulting thresholds. The distribution was the following: five participants had a threshold of one to eleven (1:11); five participants had 2:10; four participants had 3:9; five had 4:8; fifteen had a threshold of 5:7.

Event-Related Potentials

To determine if there were differences in the ERPs related to condition or stimulus, a 2 (condition: IDM, EDM) x 2 (stimulus: Individualised, Shared) repeated measures ANOVA on the peak amplitudes for both components was calculated (Fig 2).

In the early component, there was a significant effect of stimulus (Wilks' Lambda = .639, $F(1,33) = 18.670$, $p < .000$), but not of condition (Wilks' Lambda = .970, $F(1,33) = 1.028$, $p = .318$)(Fig 2A, B). The same results were found in the late component. There was a significant effect of stimulus (Wilks' Lambda = .790, $F(1,33) = 8.771$, $p = .006$), while no

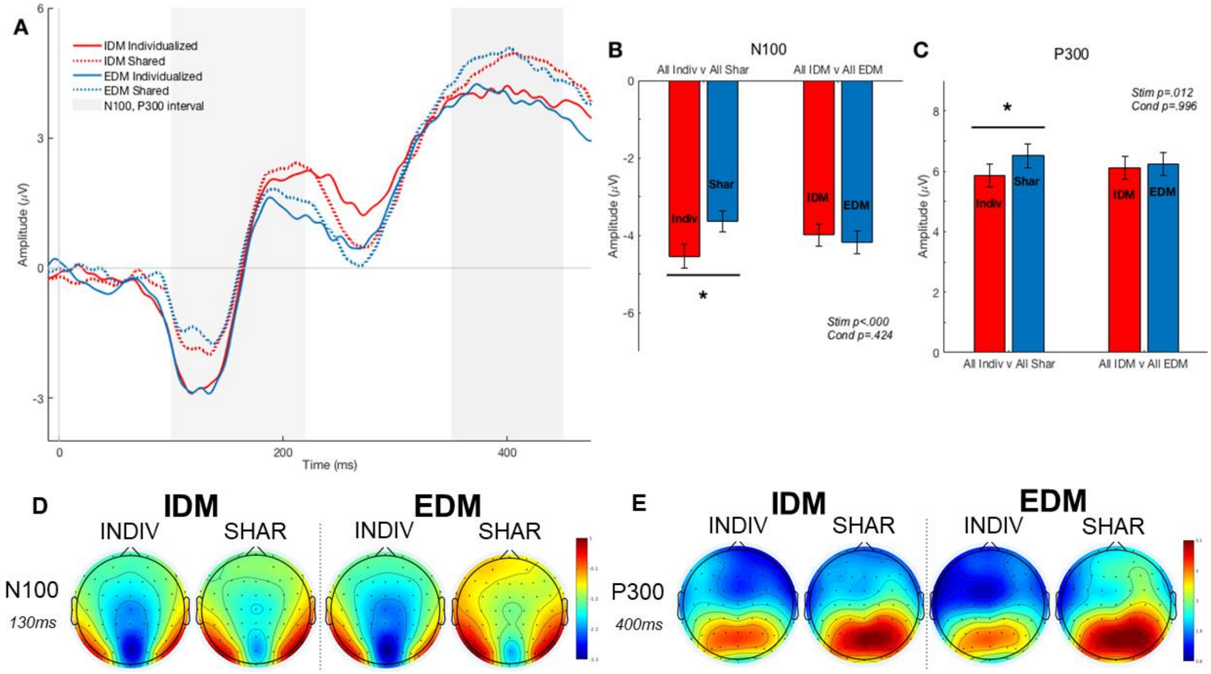


***Figure 2**: Event-related potentials (ERPs) at electrode Pz. **A)** Early N100 and late P300 ERP components. **B)** The minimum amplitude between 100ms and 220ms was measured for the N100 while the maximum amplitude between 350ms to 450ms was measured for the P300. When all individualized stimuli were compared with all shared in the early component, a significant effect of stimulus was found (p < .000). When all IDM stimuli were compared with all EDM, no significant effect of condition was found (p = .424). **C)** The same results were found in the late component, with a significant effect of stimulus (p = .012), but no significant effect of condition (p = .996). D) Topographical maps for the N100 component at 130ms. **E)** Topographical maps for the P300 component at 400ms. P-values are Benjamini-Hochberg FDR corrected for multiple comparisons.*

such difference was seen between conditions (Wilks' Lambda = 1.000, *F*(1,33) = .000, *p* = .996)(Fig 2A, C).

In sum, peak activity from individualized stimuli was significantly greater than shared in the N100, while the opposite was found in the P300.

Event-Related Spectral Perturbation

From the significant ERP findings, we sought to measure changes in the frequency power due to stimulus onset. To do so, the event-related spectral perturbation (ERSP) between stimuli for each condition was measured. There was a significant effect of

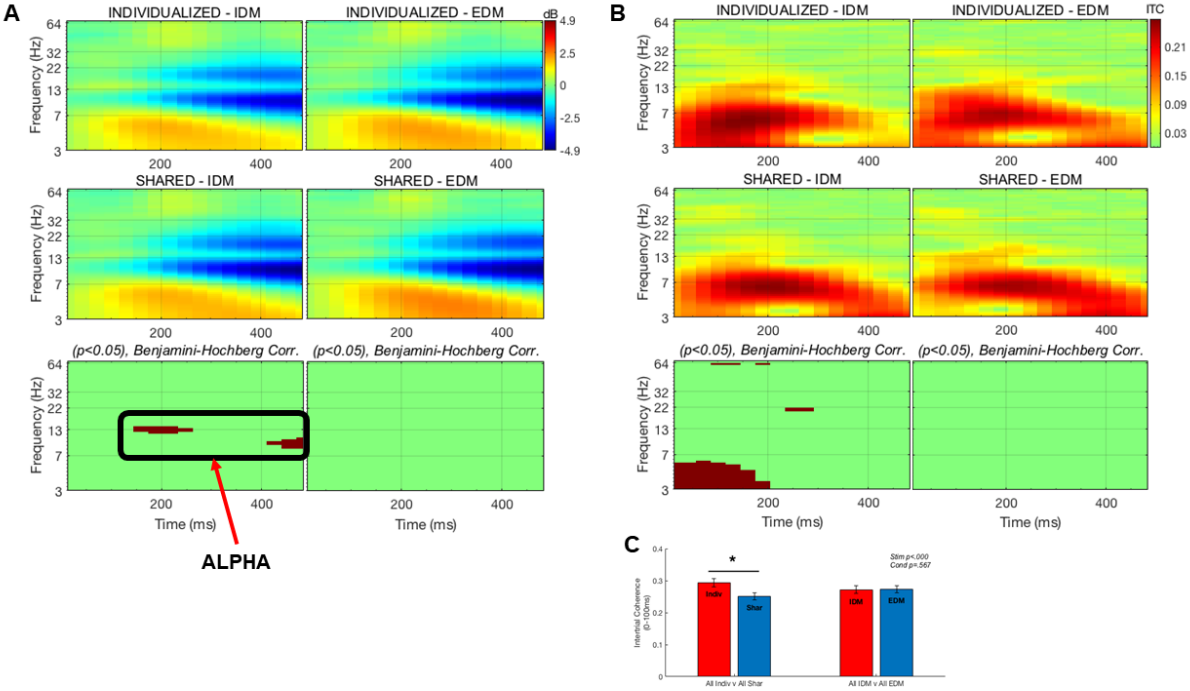


__Figure 3__: Event-related spectral perturbation (ERSP) and intertrial coherence (ITC) of individualized and shared stimuli in both conditions at electrode Pz. __A)__ There was a significant effect of stimulus between 140ms to 263ms and 415ms to 500ms in the alpha band in the IDM condition. __B)__ There was a significant difference between individualized and shared stimuli in the IDM condition between 3-6Hz from stimulus onset to 200ms. __C)__ The first 100ms of ITC for each stimulus in each participant was further analyzed for both stimulus and condition related effects. There was a significant effect of stimulus on ITC, but not of condition. P-values are Benjamini-Hochberg FDR corrected for multiple comparisons.

stimulus for the following time intervals: from 140 to 263ms between 11.5-14Hz, and between 8.5-10.5Hz from 415 to 500ms in the IDM condition (Fig 3A).

Therefore, a difference in alpha power between individualized and shared stimuli was found in the IDM condition.

Intertrial coherence

After finding significant differences in frequency power, we next wanted to examine the effect of stimuli and condition on phase. To examine phase consistency across trials, intertrial coherence (ITC) between stimuli was measured.

There was a significant difference between 3-6Hz from stimulus onset to 200ms (Fig 3B). Next, to determine if there was a significant effect of stimulus or condition on all stimuli, the first 100ms of ITC for each stimulus in each participant was extracted (Fig 3C). This time range was chosen due to the significant results found in the ITC analysis in Figure 3B. The frequency range was also from the significant ITC results, and those specific frequencies were the datapoints nearest to the whole numbers in which we found results (there was no datapoint for 4Hz, so 3.92Hz was the nearest datapoint).

This data was analyzed in the same way as the ERP amplitude values, using a 2 (condition: IDM, EDM) x 2 (stimulus: Individualized, Shared) repeated measures ANOVA. It was found that there was a significant effect of stimulus (Wilks' Lambda = .573, $F(1,33) = 24.558$, $p < .000$), but not of condition, (Wilks' Lambda = .990, $F(1,33) = .334$, $p = .567$).

Taken together, delta/theta ITC was significantly different between stimuli - individualized vs shared - but not between conditions - IDM vs EDM.

TTV index

To measure the variability across trials related to stimulus onset, a new index, the trial-to-trial variability (TTV) index, was calculated. The TTV index – TTV in the actual trials minus TTV in the pseudotrials - was calculated in broadband and each individual frequency band to measure neural variability quenching related to stimulus onset.

For each frequency band, a 2 (condition: IDM, EDM) x 2 (stimulus: Individualized, Shared) repeated measures ANOVA was calculated to determine if there was an effect

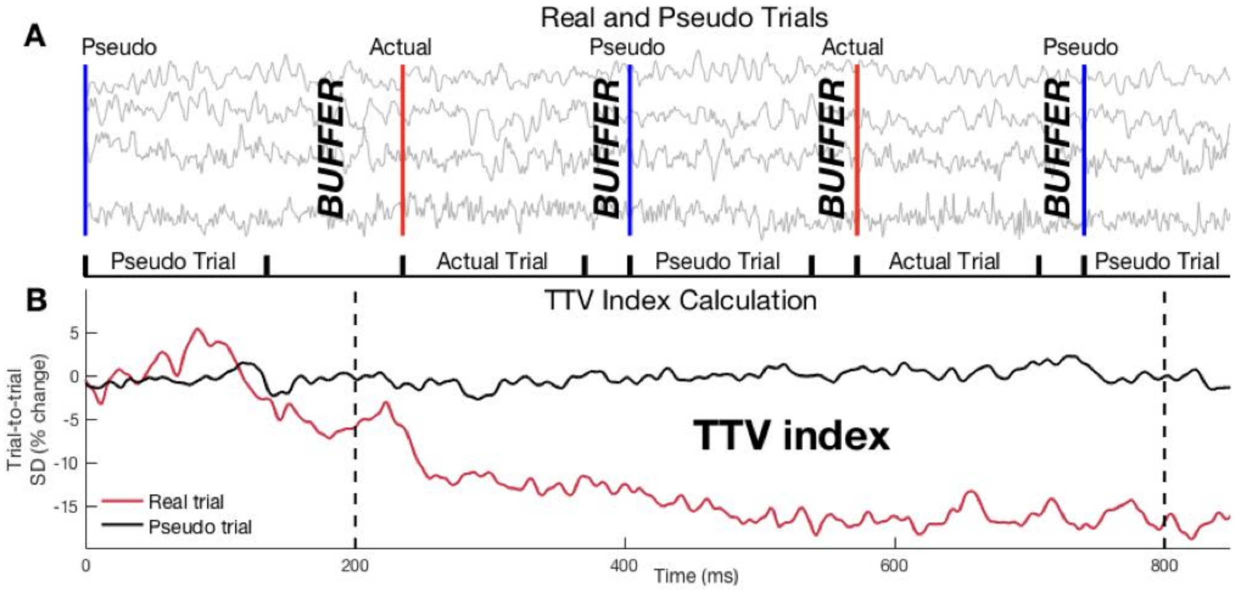


Figure 4: *Pseudotrial placement and trial-to-trial variability (TTV) index calculation.* ***A)*** *Pseudotrials are calculated from periods of the intertrial intervals (ITIs) in which a virtual stimulus was inserted. For a 5s ITI, the pseudo stimulus onset was inserted 3.5s prior to the actual stimulus onset. Before this, a 1s buffer between the actual trial and the pseudotrial was taken, with the pseudo stimulus onset (0ms) in the 5s ITI inserted 3.5s prior to the actual stimulus. In the 5.5s and 6s ITI's, the buffer between the pseudotrial and the actual trial increased from 1s in the shortest ITI to 1.5s and 2s in the longest. From the pseudotrials, TTV of this pseudo (or surrogate) stimulus was then calculated in the same way as with the actual stimulus (see Huang et al, 2017 for a similar method in fMRI).* ***B)*** *To account for the change in variability specifically related to the stimulus itself, the pseudotrial TTV was subtracted from the actual trial TTV from 200 to 800ms poststimulus. The mean was then calculated yielding one value, the TTV index. The pseudotrial was subtracted to account to the ongoing spontaneous fluctuations of the neural activity.*

of condition or stimulus. Neither the stimulus (Wilks' Lambda = .972, *F*(1,33) = .968, *p* = .332), nor the condition (Wilks' Lambda = .924, *F*(1,33) = 2.708, *p* = .109) had significant effects in the broadband. The same was found in the theta band (Wilks' Lambda = .984, *F*(1,33) = .553, *p* = .462, and (Wilks' Lambda = .946, *F*(1,33) = .1.874, *p* = .180, respectively)(Sup Mat).

In contrast, in the alpha band there was a significant effect of stimulus (Wilks' Lambda = .815, *F*(1,33) = 7.258, *p* = .011) but not of condition (Wilks' Lambda = .999, *F*(1,33) = .035, *p* = .854)(Fig 5B). The same was found for the beta band, with a significant effect of stimulus only (Wilks' Lambda = .856, *F*(1,33) = 5.556, *p* = .025, and Wilks' Lambda = .996, *F*(1,33) = .149, *p* = .702, respectively)(Fig 5C).

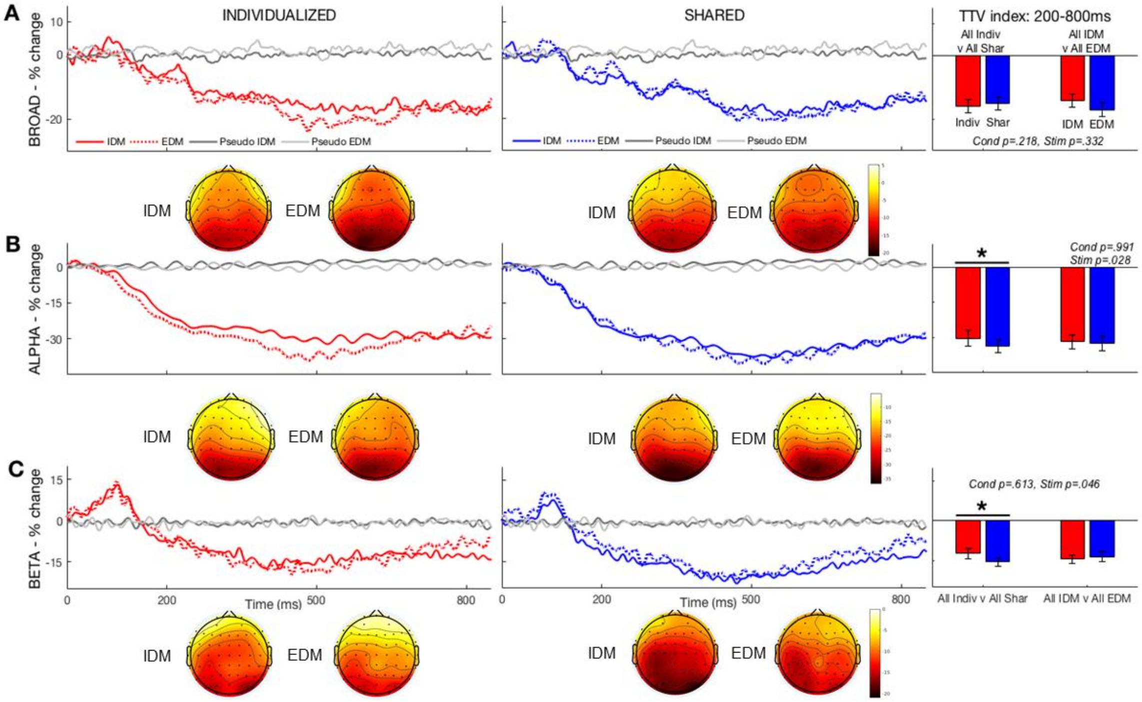


***Figure 5**: Trial-to-trial variability (TTV) index for both stimuli and conditions at Pz. **A)** TTV in the broadband (0.5-70Hz) grouped according to stimulus. Topographical maps for the broadband are below each TTV curve. **B), C)** When the TTV indices for each frequency band were grouped by stimulus (left bars) and condition (right bars), there was found to be a significant effect of stimulus in the alpha (B) and beta (C) bands. Columns = stimulus: individualized (left column); shared (center column); bar plots of TTV index values by stimulus and condition (right column). Rows = frequency bands: broadband of 0.5-70Hz (top row); alpha between 8-13Hz (middle row); beta between 13-30Hz (bottom row). Statistics for bar graphs are from a 2x2 repeated measures ANOVA. P-values are Benjamini-Hochberg corrected for multiple comparisons.*

To determine if this significant difference existed only at electrode Pz, an adjacent electrode, POz – still in the centroparietal area – was analyzed with the TTV index in the same two bands. Again, a significant difference between individualized and shared stimuli (Wilks' Lambda = .819, *F*(1,33) = 7.295, *p* = .011, and Wilks' Lambda = .856, *F*(1,33) = 5.556, *p* = .025) was found in the alpha and beta bands respectively.

Lastly, in the gamma band, neither stimulus (Wilks' Lambda = .988, *F*(1,33) = .412, *p* = .525) nor condition (Wilks' Lambda = .967, *F*(1,33) = 1.110, *p* = .300) had a significant effect on TTV index (Sup Mats).

In sum, there was a significant effect of stimulus - individualized vs shared - only in the alpha and beta bands of the TTV index. This features the TTV index as a marker of individuality on the neural level.

Effect of Threshold on TTV index and reaction times

After calculating the above TTV index results, and upon visualization of the data, the effect of threshold on TTV index only in the significant frequency bands was examined. For both alpha and beta, and individualized and shared, a 2 (condition: IDM, EDM) x 2 (stimulus: Individualized, Shared) x 3 (threshold: low, middle, high) repeated measures ANOVA, with between subjects' factor of threshold was performed. As the 2x2 statistics were identical to the above values, and the test was done to determine if there was an interaction with the threshold, the statistical values were ignored.

A significant interaction (condition, threshold) was found in the alpha band, ($F(2) = 4.154$, $p = .026$), but not in the beta band ($F(2) = .789$, $p = .463$)(Fig 6A). There was no significant effect of threshold in either band.

Next, to link the TTV index to behavioural measures, correlations were done between the difference of mean reaction times and the difference of TTV indices in alpha and beta bands. The correlation was significant in the beta band ($\rho = .461$, $p = .004$) (Fig 6B) in the IDM condition, but not in the alpha band ($\rho = .321$, $p = 0.099$). Neither the beta ($\rho = -.119$, $p = 0.261$) nor the alpha band correlations ($\rho = -.257$, $p = 0.162$) were significant in the EDM condition.

In brief, there was a significant effect of threshold on the TTV index in the individualized stimuli of the alpha band, while there was a significant relationship with reaction time in

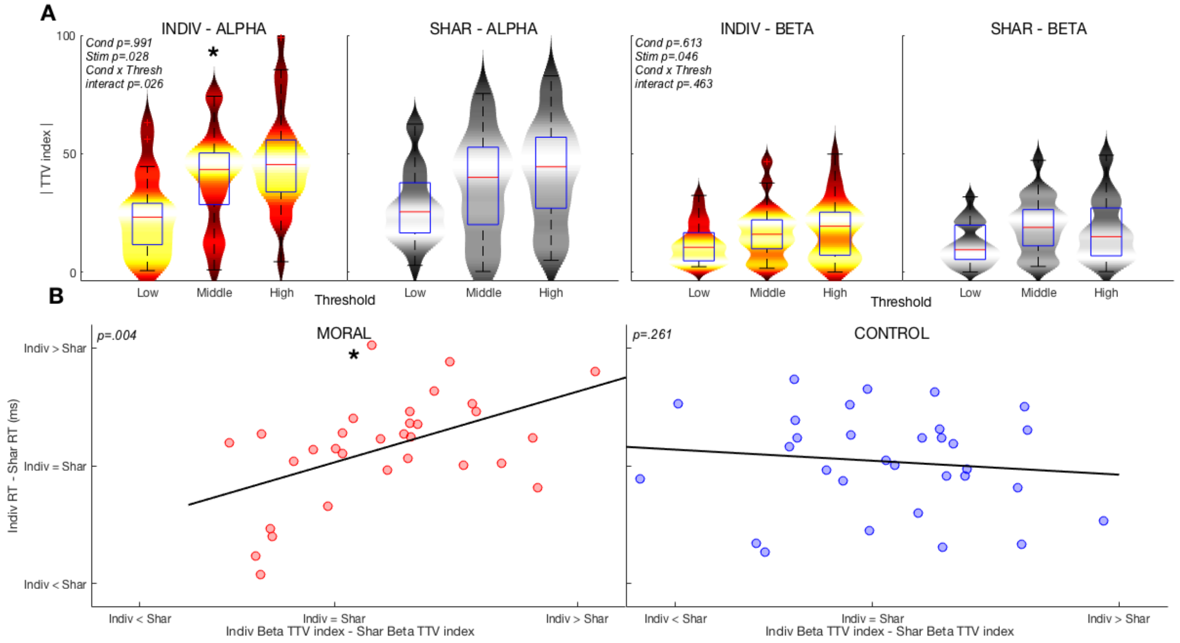


Figure 6*: The effect of threshold on trial-to-trial variability (TTV) index and TTV index correlations with reaction time.* ***A)*** *In a 2x2x3 ANOVA (between subjects' factor is threshold) with three levels (low, middle, high threshold had a significant interaction on the absolute value of the TTV index in individualized stimuli in the alpha band, but not in the beta band. The TTV index values are grouped according to stimulus, not conditions, for both bands only for reasons of illustration.* ***B)*** *In order to focus on the differences related to stimulus, the differences between mean reaction times (individualized minus shared stimuli) and the TTV index in the beta band were correlated. There was a significant correlation in the IDM condition. P-values are Benjamini-Hochberg corrected for multiple comparisons.*

the beta band in the IDM condition. Both findings underline the relevance of TTV for individuality on the behavioral (reaction time) and psychological (threshold) level.

Lempel-Ziv Complexity prior to and after stimulus onset

After examining the results found in the TTV index related to alpha and beta, and after visualization of the TTV curves, it was decided to measure the complexity of the signal before and after stimulus onset to see if this measure - related to information theory - might suggest a mechanism for our TTV results. Using the LZC measure, 500ms prior

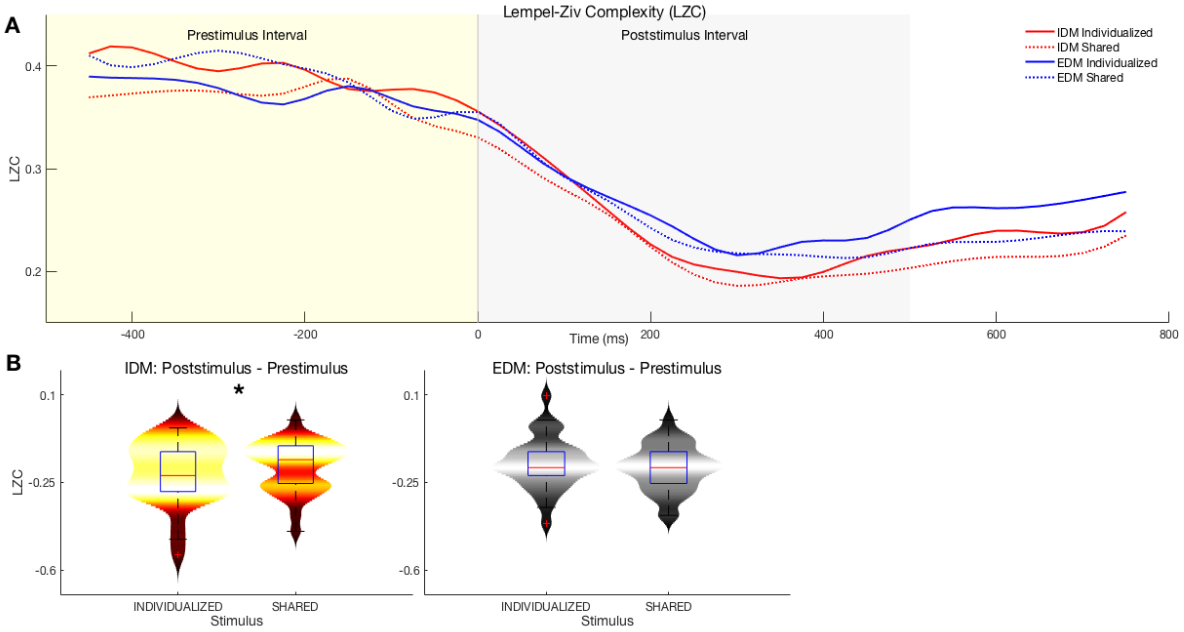


Figure 7*: Lempel-Ziv complexity (LZC) in the prestimulus and poststimulus periods.* ***A****) To examine complexity as a mechanism for TTV, 500ms prior to and after stimulus onset were investigated for complexity using the LZC measure. In paired samples t-tests, it was found that stimulus onset had a significant effect on complexity in both groups of stimuli and conditions. In contrast, there was no significant difference in the pseudotrials, which acted as surrogates. The time-resolved LZC seen here was computed for visualization only using a window of 500ms, overlap of 90%, and step of 50ms. Line curves were smoothed in MATLAB using the function spline.* ***B)*** *Two paired-samples t-tests was conducted comparing the difference in LZC related to stimulus onset between the individualized and shared stimuli in both conditions. There was a significant effect of stimulus in the IDM condition, but not in the EDM condition. P-values are Benjamini-Hochberg FDR corrected for multiple comparisons.*

to and after stimulus onset was investigated for complexity (Casali et al., 2013; Ibáñez-Molina et al., 2015; Kalev et al., 2015).

To begin with, we wanted to determine if prestimulus complexity differed from that after the stimulus appeared. Therefore, paired-samples *t*-tests were calculated for all stimuli in both conditions (Fig 7A). It was found that stimulus onset had a significant effect on complexity for all stimuli (individualized IDM: *t*(33) = 9.978, *p* = .002, shared IDM: *t*(33) =

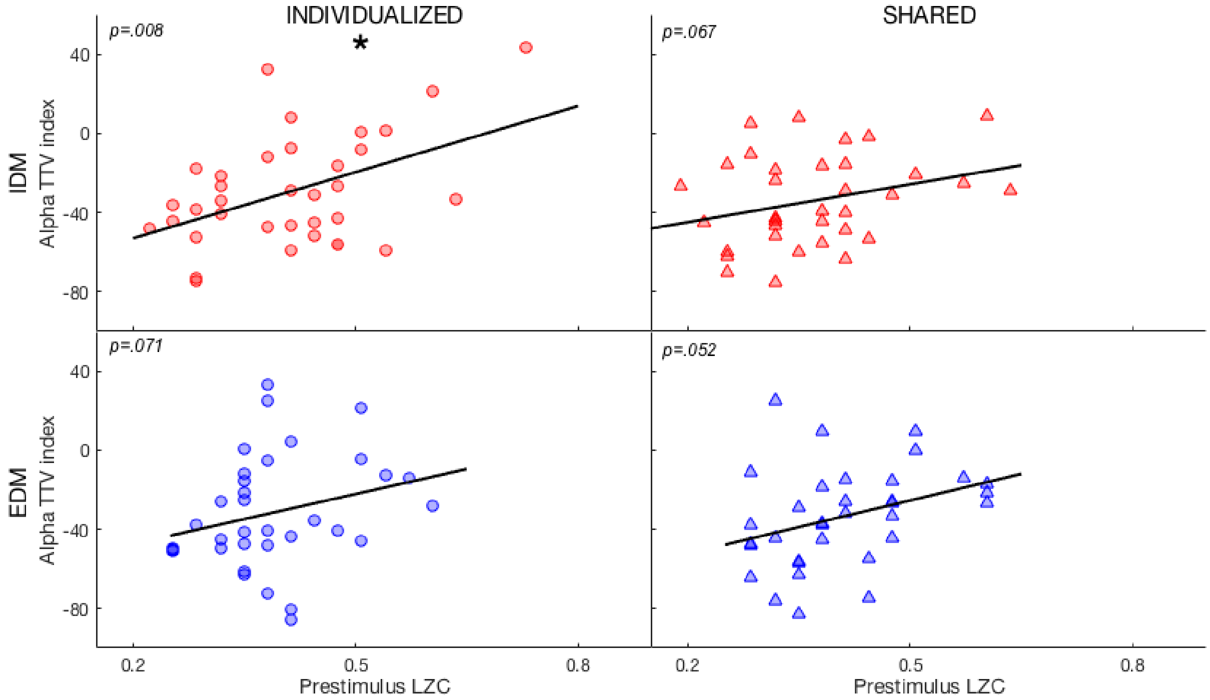


***Figure 8**: Prestimulus Lempel-Ziv complexity (LZC) correlates with alpha TTV index. To determine the relationship between prestimulus LZC on TTV index in alpha, one-tailed Pearson correlations were calculated. Significant correlations were found in the individualized stimuli in the IDM condition, not the shared. Neither the individualized nor the shared stimuli had significant correlations in the EDM condition. P-values are Benjamini-Hochberg FDR corrected for multiple comparisons.*

10.821, *p* = .002, individualized EDM: *t*(33) = 9.845, *p* = .002, shared EDM: *t*(33) = 12.354, *p* = .002). In contrast, the pseudotrials, which functioned here as surrogates for the actual trials, showed no significant difference in either condition (*t*(33) = -.950, *p* = .415, and *t*(33) = -.848, *p* = .424, respectively).

After seeing visualisations of the LZC distributions both pre- and poststimulus, a 2 (stimulus: individualized, shared) x 2 (condition: IDM, EDM) repeated measures ANOVA was done to establish if the differences seen visually between complexity before and after onset, and between conditions, were statistically significant (poststimulus complexity minus prestimulus complexity) (Fig 7B). It was found that there was no significant effect of neither condition (Wilks' Lambda = .986, *F*(1,33) = .433, *p* = .516) nor stimulus (Wilks' Lambda = .988, *F*(1,33) = .375, *p* = .545). There was, however, a significant interaction between these two factors (Wilks' Lambda = .831, *F*(1,33) = 6.087, *p* = .020).

Because of this significant interaction, two paired-sample *t*-tests were conducted on these LZC difference values, between the individualized and shared stimuli (Fig 7B). A significant effect of stimulus (*t*(33) = -2.381, *p* = .048) was found in the IDM condition, not in the EDM condition (*t*(33) = .934, *p* = .357).

Finally, to determine if prestimulus LZC was related to poststimulus TTV in alpha and beta, correlations were calculated. A significant correlation was found in the alpha band only (Fig 8). Specifically, there was a significant correlation in the individualized stimuli (*ρ* = .477, *p* = .008) of the IDM condition and not the shared stimuli (*ρ* = .287, *p* = .067). Neither the individualized (*ρ* = .257, *p* = .071) nor the shared (*ρ* = .344, *p* = .052) stimuli had significant correlations in the EDM condition.

All together, these findings show that complexity decreased after stimulus onset in all stimuli and conditions, however this pre- to poststimulus decrease was significantly different between individualized and shared stimuli in the IDM condition. In addition, a significant relationship between prestimulus complexity and TTV index in the alpha band was found in the individualized stimuli of the IDM condition. These findings suggest that pre-stimulus complexity mediates the individual features of post-stimulus TTV.

eLORETA source localization correlations with alpha and beta TTV index

To support our correlations between the alpha TTV index and prestimulus LZC and beta TTV index and reaction time, we performed correlations between these TTV indices and eLORETA source activity in the visual cortices.

There was a significant correlation between the visual cortices eLORETA activity from the individualized stimuli and the TTV index in the beta band (ρ = -.421, p = .032) in the IDM condition. The correlations for the shared IDM (ρ = -.178, p = .264), individualized EDM (ρ = -.154, p = .264), and shared EDM (ρ = -.116, p = .264) were not found to be significant. None of the correlations in the alpha band were significant (p = .104, p = .206, p = .403, and p = .212).

Finally, to determine if the significant correlation was only in the visual cortices, the same analysis was performed in the premotor cortex, the posterior cingulate cortex and the inferior parietal lobules as control regions. For activity in these ROIs, none of the correlations were significant: premotor cortex - p = .168, p = .435, p = .340, and p = .340; posterior cingulate cortex - p = .094, p = .418, p = .456, and p = .476; inferior parietal lobules - p = .094, p = .426, p = .217, and p = .268, respectively.

Table 1: Significance values for correlation between eLORETA activity (0-200ms) and beta TTV index

CORTICAL AREA	**INDIV. IDM**	**INDIV. EDM**	**SHAR. IDM**	**SHAR. EDM**
VISUAL CORTEX *(BA 17, 18)*	.032	.264	.264	.264
PREMOTOR CORTEX *(BA 6)*	.168	.340	.435	.340
POSTERIOR CINGULATE CORTEX *(BA 29/30, 23/31)*	.094	.456	.418	.476
INFERIOR PARIETAL LOBULES *(BA 39,40)*	.094	.217	.426	.268
ALL SIGNIFICANCE VALUES ARE BENJAMINI-HOCHBERG FALSE DISCOVERY RATE CORRECTED				

Together, these eLORETA source localization findings show a correlation between the beta TTV index and individualized stimuli, and that this activity was specific to the visual cortex.

Discussion

We investigated the behavioral relevance and neuronal mechanism of TTV. Applying a specific paradigm for testing internally-guided decision making, we observed that TTV, specifically in the alpha and beta bands, showed significant differences between individualized and shared stimuli in specifically IDM (as distinguished from EDM). This finding suggests that TTV can be considered a marker of the individual specifics of individual neural activity and its manifestation on psychological and behavioral levels.

Crucially, we show that TTV for individualized stimuli is related to prestimulus complexity, as measured by LZC. This suggests that individualized TTV quenching is related to a reduction of prestimulus information complexity which, as our data suggest, mediates the individual features of post-stimulus TTV. Together, our data show for the first time that TTV quenching is a highly individualized neural marker and is mediated by prestimulus information complexity.

These results carry major implications for our understanding of the behavioral relevance and neuronal mechanisms of how the more internally-based spontaneous activity, specifically prestimulus activity, interacts with external stimuli as during stimulus-induced activity.

TTV as neural marker of individuality

Arazi *et al* (Arazi et al., 2017b) demonstrated that TTV remains stable within one participant across tasks as well as over time. These results suggest that TTV is a trait marker of the individual participants and distinct from others. If this is the case and TTV is indeed a neural trait marker of individuality, one would expect that TTV responds to the individual rather than shared features of stimuli in perceptual or cognitive paradigms. To test this, we applied a novel study design of an IDM task. This allowed us to compare directly individualized stimuli to shared by individualizing the threshold of our paradigm while simultaneously controlling for task-related effects (two conditions, IDM and EDM). As expected, our behavioral data shows that participants differed in their respective thresholds as indexed by the ratios related to the IDM dilemma presented.

The neural effects of these individualized thresholds, which manifested in individualized stimuli, were then compared with those of stimuli presented to all participants. As expected, this led to significant differences in ERP (N100 and P300), ERSP (alpha band power), and ITC (delta and theta band) between individualized and shared stimuli. Notably, these differences could not be traced to task-related aspects; there were no significant differences between IDM and EDM in these measures. Our results are well in accordance with others showing analogous effects of individualized stimuli on ERP, ERSP, ITC and other measures (Houben and Wiers, 2007; Qin et al., 2008; Kessler et al., 2011, 2017; Wiswede et al., 2014; Bai et al., 2016).

As it was the main target of our study, it was of great importance that we demonstrated significant differences in TTV between individualized and shared stimuli in the alpha and beta frequency bands, specifically. Though our examination of TTV is well in accordance with the various studies in EEG/MEG (He and Zempel, 2013; Schurger et al., 2015; Arazi et al., 2017a) and fMRI (He, 2013; Ferri et al., 2015; Huang et al., 2017a, 2018), the present results add two important innovations to the growing TTV literature, first TTV is a marker of neural individualization and secondly, post-stimulus TTV is mediated by pre-stimulus information complexity.

We demonstrate that TTV effects are related to the individual neural response to a stimulus. While previous studies showed interindividual differences in TTV (Ferri et al., 2015; Arazi et al., 2017a, 2017b), here we tested the hypothesis of TTV as an individual neural marker by comparing individualized and shared stimuli directly. This approach yielded significant differences in TTV related to stimulus, specifically in the alpha and beta bands (other bands showed TTV but no differences between stimuli). In addition, the eLORETA results supported this finding with a significant correlation between the visual cortex and TTV in the beta band only in individualized stimuli.

Furthermore, the significant correlations in the individualized stimuli only in the IDM condition suggests that an aspect of the stimulus interacts with the condition. It may be that individualization is relevant only in some contexts for some measures as they require more internally oriented criteria (Nakao et al., 2012). Such findings are consistent with literature related to IDM – preference based – and EDM – objective response – decision-making (Nakao et al., 2010, 2012, 2016) as in IDM the response depends on the participants' own internal criteria as mediated by their internal pre-stimulus activity, specifically its variance and complexity. Our findings imply that in certain measures, the context of the stimulus (IDM or EDM) has a further impact on the stimulus induced activity as may occur in IDM. Further disambiguation of this, however, is required.

The special role of individualized TTV in the beta band is further supported by our finding of a significant correlation between the beta TTV index in the individualized stimuli and reaction time. Together, these findings suggest that 1) TTV represents a neural marker of individuality, and that 2) such 'neural individualization' is processed in the alpha and beta frequency bands specifically. As the need for obtaining neural markers of individualization grows in both basic and clinical neuroscience (Braver et al., 2010; Reineberg et al., 2015; Friedman and Miyake, 2016; Jang et al., 2017; Seghier and Price, 2018), we here suggest that TTV in the alpha and beta bands can provide a marker of neural individualization.

TTV is mediated by changes in information complexity from pre- to post-stimulus periods

Previous data at both the cellular (Kisley and Gerstein, 1999; Curto et al., 2009; Schurger et al., 2010; Pachitariu et al., 2015) and regional level (He, 2013; Schurger et al., 2015; Huang et al., 2017a) suggest that prestimulus activity amplitude or variance are central in mediating poststimulus TTV quenching. Despite these important results, the exact feature of prestimulus activity which mediates poststimulus TTV quenching remains unclear.

We therefore asked the following question: is poststimulus TTV also mediated by the information complexity of prestimulus activity? In a first step, we investigated the complexity - through the measurement of LZC - of both prestimulus and poststimulus activity in two 500ms intervals. LZC, and thus complexity, was significant higher in the prestimulus period in both individualized and shared stimuli. While new by itself (Ponce-Alvarez et al., 2015), this higher prestimulus complexity is in accordance with the above cited findings related to increased prestimulus activity levels or variance preceding poststimulus TTV. Together, both suggest that the higher amplitude/variance prior to stimulus onset represents a higher information complexity, which decreases after the stimulus is presented. Such a stimulus-related difference in information complexity appears to be a basic, general neural mechanism since no differences between conditions (IDM and EDM) were found.

Remarkably, we found that these high prestimulus complexity levels were related to TTV in the alpha band in individualized stimuli of the IDM condition. In contrast, no such correlation was found in shared stimuli or in EDM. These findings suggest that TTV in the alpha band in response to individualized stimuli is closely related to prestimulus information complexity. Given that in the poststimulus period both TTV and complexity were quenched - reduced compared to prestimulus levels - we suggest that a reduction in information complexity and variability during the poststimulus period are central to mediating the individual's neural response to stimuli. It has previously been shown that resting state activity interacts with task-evoked activity (Northoff et al., 2007, 2010; He, 2013; Huang et al., 2017a), and that activity during IDM overlaps with the default mode network (DMN) (Northoff et al., 2006, Nakao et al. 2012). From these findings, it has been inferred that IDM is heavily influenced by the brain's intrinsic activity (Nakao et al., 2012). Our prestimulus complexity and individualized IDM TTV findings are strongly guided by the brain's intrinsic activity - its pre-stimulus activity - which is consistent with this view, however further work is required to support this.

Broadly, our data indicate, albeit tentatively, that spontaneous prestimulus activity and stimulus-induced activity is both nonadditive (He, 2013; Huang et al., 2017a, 2018) and individualized. If an interaction were additive, one would observe increases in both TTV and complexity; following the law of variance (He, 2013), the contributions of both spontaneous activity and stimulus are added during stimulus-induced activity. Since the opposite results were found with post-stimulus decreases in both TTV and complexity, our data strongly support a nonadditive (He, 2013; Huang et al., 2017a, 2018), rather than additive (Arieli et al., 1996; Fox et al., 2006; Becker et al., 2011) model of rest-stimulus interaction. Taken together with our observation of TTV as a marker of neural individualization, we suppose that nonadditive rest-stimulus interaction is by itself individualized. This is especially supported by our finding that TTV only from individualized (but not shared) stimuli correlated with complexity (and reaction time on a behavioral level).

The mechanism of TTV reduction has previously been related to the disambiguation or clarification of stimuli which allows for better information processing in the cortex (Monier et al., 2003; Finn et al., 2007; Churchland et al., 2010; White et al., 2012). Furthermore, modeling studies have shown that variability reduction can occur from recurrent network processing; in a multi-attractor system, the stimulus presentation can stabilize one attractor thereby suppressing the transition to other attractors (Deco and Hugues, 2012; Mazzucato et al., 2015). This stabilization of one attractor reduces net neural variability by increasing the neural orderliness (Deco and Hugues, 2012; Mazzucato et al., 2015). Spike train data has also shown a similar variability reduction due to increased regularity of spike train activity (Deco and Hugues, 2012). This increased uniformity then leads to a decrease in the transfer of information - according to Shannon information theory (Shannon, 1948; Gershenson and Fernandez, 2012) – as reduced variability is associated with more structure, and hence with increased predictability in data (Gershenson and Fernandez, 2012).

This decreasing transfer of information and clarification of stimuli may be evident in the reduced complexity after stimulus onset shown here. The question, then, is do individualized stimuli reduce the neural variability less than non-individualized stimuli because of their decreased regularization of the activity? How is this related to the prestimulus spontaneous activity since reduced quenching is less deviation from resting state activity? Could early life experiences (Duncan et al., 2015) and genetic influences (Hensch, 2005) be large contributors to these mechanisms, as a recent study suggested (Arazi et al., 2017b)? This hypothesis is tentative, at best, and requires testing in future studies.

Methodological limitations

One may argue that TTV already includes prestimulus intervals indirectly, rendering calculations of both poststimulus TTV and prestimulus complexity dependent variables rather than independent. This, in turn, would render their correlation spurious. While indeed TTV is calculated in most studies in reference to stimulus onset (Ferri et al., 2015; Schurger et al., 2015; Arazi et al., 2017a, 2017b, Huang et al., 2017a, 2018), we here introduced a novel method to avoid such dependence between TTV and prestimulus measures.

We adopted the method of pseudotrials (Huang et al., 2017a), or trials when a stimulus is absent (Dinstein et al., 2015), by inserting a pseudo-stimulus into the intertrial intervals. These pseudotrials had a buffer which ensured they remained independent of the prestimulus period and actual trial offset. We then calculated TTV for such pseudotrials and subtracted them from the actual trial TTV during the poststimulus period. Such calculation of TTV thus allowed for its independence from the prestimulus period, including its manifestation at stimulus onset. This allowed us to calculate prestimulus LZC independent of poststimulus TTV which, in turn, made the correlation possible as both were independent variables.

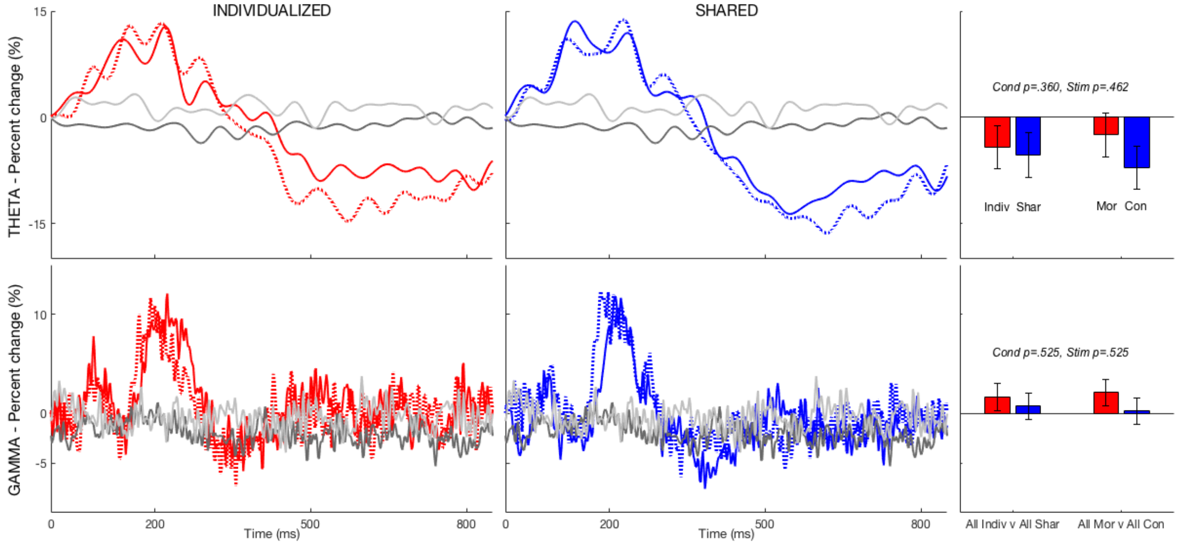
Another methodological issue consists in the lack of control for threshold proximity. The two individualized stimuli were also the ones near the threshold since the threshold defined the individualization. Presenting the participants with two stimuli that were 1) near the threshold in the same degree as the individualized stimuli, but 2) not individualized, would have been optimal controls for the proximity to the threshold. Therefore, the comparison to the individualized stimuli were stimuli presented to all participants. Their distance from the threshold (if threshold was 5:7, the shared stimuli were 1:11 and 10:2), however, was not equal.

The final study limitation relates to a lack of eye-tracking during the EEG session. Two related papers (Arazi et al., 2017a, 2017b) employed an eye-tracker while conducting their EEG study. Though we did not use this technology, we controlled for eye movements in several ways. During the study itself, the stimuli included a fixation cross at the center, and participants were seated 55-60cm away from a 34.3 x 26.7cm computer screen. This was done to minimize eye movements and the visual angle. We also used additional bipolar electrodes, placed at the outer canthi of the eyes and above and below the left eye, to measure eye movements and aid in artifact rejection during EEG preprocessing. When the data were visually inspected, all trials with blinks in the baseline period (-200ms to stimulus onset) were removed. Finally, to remove blinks and saccades in the remaining EEG data, independent component analysis (ICA) and the Multiple Artifact Rejection Algorithm (MARA) (Winkler et al., 2011, 2014) of EEGLAB (Delorme and Makeig, 2004), which standardized the artifact rejection process, were used.

Conclusion

The spontaneous activity of the brain interacts with task-evoked activity; however, the exact mechanisms of this interaction including its individually-specific nature remain unclear. We here investigated the individual behavioral relevance and neural basis of one neural marker of rest-stimulus interaction, namely trial-to-trial variability (TTV), during internally-guided decision making. As in previous studies at both the cellular and regional levels, we observed poststimulus TTV quenching which, in an extension to this previous work, was found in alpha and beta bands related to specifically individualized, but not shared, stimuli. We thus consider TTV in the alpha and beta band a marker of neural individualization. Notably, we demonstrated that TTV in the alpha band was related to prestimulus information complexity, as measured by Lempel-Ziv Complexity (LZC). Indexing internal neural activity yet unrelated to the external stimulus, pre-stimulus complexity may thus mediate the individually-specific features of TTV during the post-stimulus period on both neural and psychological levels.

Together, we demonstrate, for the first time, that poststimulus TTV quenching is a marker of ‘neural individualization’ which is mediated by prestimulus information complexity. Broadly, considering TTV as an internally-based marker of rest-stimulus interaction, these findings suggest that the interaction between the purely internal spontaneous and internal-external stimulus-induced activity is both nonadditive and individualized.



Supplementary Figure: *Trial-to-trial variability (TTV) index for both stimuli and conditions at Pz. TTV is grouped according to stimulus. Columns = stimulus: individualized (left column); shared (center column); bar plots of TTV index values by stimulus and condition (right column). Rows = frequency bands: theta between 4-8Hz (top row); gamma between 30-70Hz (bottom row). P-values are Benjamini-Hochberg corrected for multiple comparisons.*

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Article 3: The temporal signature of self: Temporal measures of resting-state EEG predict self-consciousness

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Abstract

The self is the core of our mental life. Previous investigations have demonstrated a strong neural overlap between self-related activity and resting state activity. This suggests that information about self-relatedness is encoded in our brain’s spontaneous activity. The exact neuronal mechanisms of such “rest-self containment”, however, remain unclear. The present EEG study investigated temporal measures of resting state EEG to relate them to self-consciousness. This was obtained with the self-consciousness scale (SCS) which measures Private, Public, and Social dimensions of self. We demonstrate positive correlations between Private self-consciousness and three temporal measures of resting state activity: scale-free activity as indexed by the power-law exponent (PLE), the auto-correlation window (ACW), and modulation index (MI). Specifically, higher PLE, longer ACW, and stronger MI were related to higher degrees of Private self-consciousness. Finally, conducting eLORETA for spatial tomography, we found significant correlation of Private self-consciousness with activity in cortical midline structures such as the perigenual anterior cingulate cortex and posterior cingulate cortex. These results were reinforced with a data-driven analysis; a machine learning algorithm accurately predicted an individual as having a “high” or “low” Private self-consciousness score based on these measures of the brain’s spatiotemporal structure. In conclusion, our results demonstrate that Private self-consciousness is related to the temporal structure of resting state activity as featured by temporal nestedness (PLE), temporal continuity (ACW), and temporal integration (MI). Our results support the hypothesis that self-related information is temporally contained

in the brain's resting state. "Rest-self containment" can thus be featured by a temporal signature.

Introduction

From the resting state's temporal signature to the self

The self and its neural correlates have been extensively investigated in neuroscience. Several lines of research show that the self is associated strongly - though not exclusively - with neural activity, especially in the cortical midline structures (CMS) (Northoff and Heinzel, 2006; Murray et al., 2012, 2015; Hu et al., 2016; Sui and Humphreys, 2016). Most interestingly, various studies observed neural overlap between self-related activity and spontaneous activity in CMS (D'Argembeau et al., 2005; Schneider et al., 2008; Qin and Northoff, 2011; Whitfield-Gabrieli and Ford, 2012; Bai et al., 2015; Davey et al., 2016; Huang et al., 2016; Qin et al., 2016). Such "rest-self overlap" suggests that information about the self can be represented (Sui and Humphreys, 2016) in the resting state activity, which is known as "rest-self containment" (Northoff, 2016b). The exact neuronal mechanisms of such "rest-self containment", however, remain unclear.

There is evidence that the brain's spontaneous activity shows an elaborate spatiotemporal structure. Various neural networks, including the default-mode network (DMN), have been described on the spatial side (Yeo et al., 2011; Power et al., 2013). On the temporal side, spontaneous activity shows fluctuations and oscillations in different frequencies, ranging from infraslow (0.01 - 0.1Hz), over slow (0.1 - 1Hz), to faster (1-240Hz) frequencies (Buzsáki and Draguhn, 2004; Buzsáki, 2007). Moreover, slower frequencies show much stronger power than faster ones. Together, these two characteristics – fluctuations in spontaneous activity at different frequencies and slower frequencies having more power than faster ones - obey what is described as scale-free properties (Linkenkaer-Hansen et al., 2001; He, 2011, 2013, 2014, Huang et al., 2016, 2017a). This can be measured using the power law exponent (PLE) in the frequency domain.

Scale-free properties indicate fractal organisation where the faster frequencies are nested within the more powerful slower ones – this amounts to ‘temporal nestedness’. Such temporal nestedness on the neuronal level may also be relevant on the psychological level of the self. As the self is preserved and manifested in both shorter and longer time scales, ranging from milliseconds over hours and weeks to years and decades, one would suspect ‘temporal nestedness’ to hold on the psychological level. This has been supported by a recent study of ours which demonstrated a relation between scale-free properties and Private self-consciousness in the infraslow frequency range, as obtained with fMRI (Huang et al., 2016). In contrast, the relation of the EEG-based faster frequencies’ temporal nestedness, their scale-free properties (1-40Hz), with the self remains unclear.

Yet another measure of the temporal structure of spontaneous activity is the autocorrelation window (ACW) (Honey et al., 2012; Murray et al., 2014). Simply put, the ACW measures the correlation in neural activity patterns across different points in a time series; the stronger the correlation between distant points in time, the longer the ACW. It thus indexes sameness or ‘temporal continuity’ of neural activity. It is still unclear how such ‘temporal continuity’ on the neuronal level is related to the self on the psychological level. This is of high interest given that, on a psychological level, our self can be characterized by temporal continuity as we perceive ourselves in an extended way (Ersner-Hershfield et al., 2009b, 2009a; Northoff, 2017). The relationship between temporal continuity on the neuronal level and the psychological level of self-consciousness remains unclear though.

In addition to the temporal nestedness of scale-free properties and the temporal continuity of the ACW, spontaneous activity also shows coupling between different frequencies. This amounts to cross-frequency coupling (CFC) (Lakatos et al., 2008; Tort et al., 2008; Canolty et al., 2009; He et al., 2010; Aru et al., 2015; Hyafil et al., 2015; Bonnefond et al., 2017). CFC can be quantified by measuring the modulation index (MI) of the signal (Canolty and Knight, 2010; He et al., 2010). The CFC refers to dynamic interactions between oscillations in the brain that operate at different frequency bands (Hyafil et al., 2015). This has been shown in both slow and fast frequencies (Buzsáki et al., 2013; Aru et al., 2015; Hyafil et al., 2015), and in the infraslow ranges (Huang et al., 2017a). CFC demonstrates the relationship between varying neural oscillations, thus allowing for what is described as ‘temporal integration’. It is still unclear, however, how such temporal integration of different frequencies is related to the self.

The question of temporal integration becomes even more powerful given that, on a psychological level, the self has been associated with the integration of different functions: sensory (Sui et al., 2012, 2013), motor (Frings, C. & Wentura, 2014), affective (Northoff et al., 2009), cognitive (Nakao et al., 2012, 2013a, 2016), and social (Schilbach et al., 2013). Strikingly, these functions operate in different frequency ranges (Buzsáki, 2007) and their integration on the psychological level may ultimately be traced to temporal integration on the neuronal level. Therefore, what on the psychological level is described as the integrative function of the self may, on the neuronal level, be realized by temporal integration of different frequencies as mediated by CFC. One would consequently expect resting state CFC (as measured by MI) to predict the degree of self-consciousness. That is yet to be investigated.

Taken together, there is strong empirical evidence that (i) the brain’s resting state activity - its spontaneous activity - is closely related to our sense of self, or self-consciousness (Qin and Northoff, 2011; Davey et al., 2016; Northoff, 2016b); and that (ii) on a purely psychological level, the self can be characterized by strong temporal integration which includes temporal nestedness (manifest over different time scales or frequency ranges), temporal continuity (as in self-continuity), and temporal integration (as in the integrative function of self). Aiming to bridge the gap between psychological and neuronal levels, we therefore applied measures to the brain’s spontaneous activity, specifically the PLE, ACW, and CFC, which index those psychological temporal features - temporal nestedness, continuity, and integration - on the neuronal level and we correlated them with self-consciousness.

Aims and Hypotheses

The main and overarching aim of our study was to investigate how the various measures of the resting state’s temporal signatures are related to self-consciousness. For that purpose, we conducted resting state EEG with eyes closed (EC). The resting state’s temporal signature was analysed in a whole-brain manner with measures for temporal nestedness (scale-free activity as with PLE), temporal continuity (the ACW), and temporal integration (CFC as measured with MI). The same participants also underwent psychological assessment of their self with the self-consciousness scale (SCS) which includes Private, Public and Social subscales (Fenigstein et al., 1975; Scheier and Carver, 1985; Abe and Bagozzi, 1996). Generally, we hypothesized a direct relationship between the various measures of the resting state's temporal signature and Private self-consciousness. This was further tested by applying machine learning as a data-driven method of validation.

The first specific aim was to measure the resting state's temporal nestedness through its scale-free properties and relate them to self-consciousness. In one of our previous fMRI studies (Huang et al., 2016), it was found that the PLE in the infraslow frequency range (0.01 to 0.1Hz) in the medial prefrontal cortex correlated significantly with the Private self-consciousness scale subscore, while the Public and Social subscores did not. Based on these previous fMRI results, we hypothesized that higher degrees of scale-free properties in the resting state as measured by the power law exponent are related to higher degrees of Private self-consciousness (as distinguished from Public and Social self-consciousness).

The second specific aim was to measure the resting state's temporal continuity through the ACW and relate it to self-consciousness. Based on the strong determination of ACW by slower frequencies specifically (Honey et al., 2012), and the finding that the infraslow frequencies (in fMRI) correlated with private self-consciousness (Huang et al., 2016), we hypothesized that a longer ACW was related to both higher degrees of scale-free activity and Private self-consciousness.

The third specific aim was to associate the resting state's temporal integration with self-consciousness. This was done by examining CFC as measured by modulation index (MI). Based on the close link between scale-free properties and cross-frequency coupling (He et al., 2010; He, 2014) with strong impact of the slow frequencies on both CFC (He et al., 2010) and private self-consciousness (Huang et al., 2016), we hypothesized that higher degrees of MI are related neuronally to higher degrees of PLE and ACW, and psychologically to stronger Private self-consciousness.

Using eLORETA for topographical analyses, our fourth specific aim was to test for the relevance of EEG-based resting state activity in cortical midline structures such as the perigenual anterior cingulate cortex (pACC) and posterior cingulate cortex (PCC) for self-consciousness. Based on previous results (Northoff et al., 2006; Davey et al., 2016; Huang et al., 2016), we hypothesized that the degree of EEG-based resting state activity in pACC/PCC (as measured by eLORETA values) is related to the degree of Private self-consciousness.

Finally, we wanted to evaluate the relationship between PLE, ACW, MI and eLORETA values for determining the SCS scores using a data-driven approach. For this, we employed a supervised classifier. A classifier is a system that divides data into different classes, by learning the relationship between the selected features and the selected classes. Specifically, we used a Support Vector Machine (SVM), which is a popular and useful classifier algorithm, to do this. As this was a data-driven analysis we did not have an *a priori* hypothesis, but rather we used it to supplement our other findings.

Materials and Methods

Subjects

Fifty (25 female) healthy subjects were included in the subsequent analysis. Sixty participants completed the resting state session. Of these, four were excluded due to technical issues related to EEG recording and three were excluded due to excessive movements during the resting state session. A further three participants tested positive for marijuana through the E-Z Split Key cup 5 (testing for marijuana, opiates, cocaine, methamphetamine, and phencyclidine). This urine drug test was performed the day of the EEG session as part of an adjacent study. Due to the possibility that the drug would affect the EEG data (Banoczi, 2005), their data was excluded from all analyses.

All participants were between the ages of 18 and 55 and were right-handed as per the Edinburgh Handedness Tool (Oldfield, 1971). The Handedness Tool subscores were the following: Writing had a mean of 100, and standard deviation (SD) of 0; Throwing had a mean of 90.24 and SD of 20.06; Toothbrush had a mean of 87.80 and a SD of 26.88; Spoon had a mean of 91.46 and SD of 19.05; Laterality Quotient had a mean of 92.38 and SD of 11.48. Participants completed a self-report health questionnaire in which all reported no history of neurological or psychiatric diagnosis, no history of concussion or other head injury, and no history or current use of substances of abuse. The experimental protocol was approved by the research ethics committee of the University of Ottawa Institute of Mental Health Research, and the study was carried out with their permission. Written informed consent was obtained from each participant prior to study participation.

Self-Consciousness Scale

The Self-Consciousness Scale (SCS) (Fenigstein et al., 1975; Scheier and Carver, 1985; Abe and Bagozzi, 1996), a twenty item self-report questionnaire, investigates the concept of the self. It breaks this ambiguous concept down into three concrete dimensions: Private, Public and Social self-consciousness. Each of these dimensions is a subscale which is comprised of responses from six questions.

The Private subscale is concerned with thoughts and reflections about oneself, while the Public subscale concerns oneself in interactions with others in the Public arena (Fenigstein et al., 1975). The Social subscale, on the other hand, relates to Social anxiety; its questions concern feelings of discomfort while in the presence of others (Abe and Bagozzi, 1996).

All participants completed the SCS prior to the EEG resting state session, and the subscale scores were calculated after the session according to the scoring key. All remaining correlations between resting state measures were one-tailed bootstrapped correlations based on 1000 samples.

Electrophysiological recording

EEG data was recorded using a Neuroscan amplifier (Compumedics Neuroscan, Charlotte, NC, USA) and Ag/AgCl electrodes through a 64-channel cap (according to the International Ten-Twenty System) referenced to the right mastoid. The data was sampled at 1000 Hz with DC recording. The impedance of each electrode was kept under 5 KΩ. An electrooculogram was recorded for each participant with a pair of electrodes above and below the right eye, and another pair on the outer canthi of each eye. The EEG data pre-processing was preformed using the EEGLAB toolbox for MATLAB. The CB1 and CB2 channels were deleted from the data because of irrelevance, and the data was referenced to two mastoid channels (M1 and M2). The data was filtered with a low-pass filter at 40 Hz and a high-pass filter at 1 Hz.

Five minutes of eyes closed resting-state data was recorded, with the participant sitting down. From this five minutes, four uninterrupted minutes in which no data had been cut out (due to artifacts) was extracted. All subsequent analyses were done on this four uninterrupted minutes.

Artifact Rejection

Artifacts such as eye blinks and muscle related potentials were left in the data for the independent component analysis (ICA). The ICA was performed via EEGLAB software on the data to create 62 ICs. A visual inspection of the ICs determined which components were the result of electrode and physiological noise. Rejection was based on time course data. As stated above, from the five minutes of eyes closed resting-state data recorded, four uninterrupted minutes was extracted and used in all subsequent analyses.

Power and Power Law Exponent (PLE) Analysis

The power law exponent was calculated using an in-house MATLAB script according to the methods of previous papers (He, 2011, 2014; Huang et al., 2016). First, uninterrupted data files of 4 minutes underwent a windowed Fast Fourier Transform (FFT). The window length was 2000ms, the window overlap was 50%, and the number of points used in the FFT was 120,000. One FFT was extracted per window before averaging them. This averaged FFT was log-log transformed in both the frequency range (1-40Hz) and power spectrum according to previous studies (Bullmore and Sporns, 2009; He et al., 2010; Huang et al., 2016). MATLAB's *polyfit* function was then used to do a linear fit between the log-log transform, and the slope of this line was extracted as the PLE value. One PLE value was extracted per channel, and the mean of all channels was used in all subsequent analyses.

Absolute power was extracted for each of the bands (delta 1-4Hz, theta 4-8Hz, alpha 8-12 z, and beta 13-30Hz) separately, also using a custom MATLAB script. They were then partially correlated with all three self-consciousness subscores. This was done to determine if the power of any one band correlated significantly with the subscores, and it was this power that was responsible for the significant correlations with the PLE.

Autocorrelation Window (ACW)

The autocorrelation window (ACW) was calculated in MATLAB (v2016a) using custom scripts according to Honey 2012. The ACW is defined as the full-width-at-half-maximum of the autocorrelation function (Fig 3A) for the EEG time course. It estimates the width of the mean lobe of the autocorrelation.

To calculate the ACW, we examined the autocorrelation function at the following lag-times: 0.1s, 0.5s and 1.0s. The number of steps for all three lag-times was 23, though the 0.1s lag computed 101 coefficients, 0.5s lag computed 501 coefficients, and 1.0s lag computed 1001 coefficients. The ACW values (Fig 3B) computed for all three lag-times agreed.

All data was sampled at 500Hz, the size of the window was 20 seconds, and the overlap of the window was 50%.

Modulation Index (MI)

The modulation index (MI) was calculated in MATLAB (v2016a) using custom scripts according to Canolty 2006, Tort 2010, and Richter 2017. The MI measures the intensity of phase amplitude coupling between the nested and nesting frequencies during the time interval being examined (Tort et al., 2010). In this study, the MI was calculated for the full four-minute Eyes Closed resting state for each participant, with delta (1-4Hz) as the 'phase-modulating' band, and all other frequencies (4-40Hz) as the 'amplitude-modulated' band. Specifically, as done in previous papers (Tort et al., 2010; Richter et al., 2017), the signal – each EEG channel here – was first filtered at the phase (1-4Hz) and the amplitude (4-40Hz) frequencies to extract filtered signals. The Hilbert transform was then applied to both the phase and amplitude filtered signals to obtain timeseries of the phases and amplitude envelope, respectively. The composite timeseries of both filtered signals was constructed and the phases of this composite were binned. The mean of the filtered amplitude signal in each phase bin was calculated. Finally, this mean amplitude was normalized by dividing it by the sum over all the bins.

Exact Low-Resolution Brain Electromagnetic Tomography (eLORETA) Analysis

Low-resolution brain electromagnetic tomography (LORETA) is a source analysis technique which aims to estimate the location and activity of the neural generators which give rise of EEG activity recorded at the scalp. Known as the inverse problem, the goal is to determine the most probable source of the EEG activity. There are several methods to resolve this problem, however LORETA is one approach which provides a linear solution to the question of where in the cortex is the source of the EEG activity recorded at the scalp.

It was developed at the KEY Institute for Brain-Mind Research at the University of Zurich (Pascual-Marqui et al., 1994) to compute the three-dimensional intracerebral distribution of neural current density sources. eLORETA (exact Low-Resolution Brain Electromagnetic Tomography) is a refinement of the original sLORETA method. It does not require standardization for correct localization (Pascual-Marqui, 2007) and is more precise in the location of the probable current density sources. When eLORETA is measured in specific brain regions as done here, the current density, based on the configuration of the EEG electrodes and the activity recorded at each of these electrodes, is computed. Since it is a current, the calculated values can be positive or negative.

The current implementation of eLORETA uses a realistic head model (Fuchs, 2002) and electrode coordinates (Jurcak et al., 2007). The 4-minute artifact-free blocks were exported into text files from the EEGLAB software for eLORETA analysis. The steps to calculate eLORETA values were as follows: (1) computing EEG cross-spectra from the raw 64-channel EEG recordings; (2) computing cortical generators of surface oscillatory activity using the cross-spectra; and (3) computing these values for the region of interest (ROI) voxels, according to Huang 2016. Here the ROI was defined as PCC and pACC using all voxels within 12cm of the following seeds (MNI coordinates):

	X	Y	Z
PCC:	-5/5	-54	22
PACC:	-5/5	47	11

Statistical Correlations

For each resting-state measure (PLE, ACW, MI, eLORETA), three partial correlations were performed, with Private, Public and Social subscores. The other two subscores were controlled for in the partial correlations. In addition, to examine the relationship between resting state measures, and for the control correlations with the power of each frequency band, one-tailed bootstrapped correlations (1000 samples) were carried out.

For all correlations, partial or bivariate, the Pearson correlation coefficient was measured since the relationship between the resting-state measure and the SCS subscores was expected to be linear. Though PLE is a nonlinear measure, the relationship between the PLE and SCS scores, which the correlations measure, is linear (Huang et al., 2016) in that they are related by the equation $y = mx + b$, with m being the slope of the line. The significance level for each of the correlations is .05.

To account for the multiple correlations performed in this study, the Benjamini-Hochberg False Discovery Rate (FDR) (Benjamini and Hochberg, 1995) was applied to all *p*-values, as was done in recent papers (Arazi et al., 2017b; Cruzat et al., 2018; Huang et al., 2018). All statistical tests from the study were listed together and the FDR was applied to all *p*-values at once. Therefore, the *p*-values in the results and figures are FDR corrected for multiple comparisons.

Support Vector Machine (SVM)

The LibSVM MATLAB toolbox (Version 3.22) was used as an implementation of the SVM algorithms (Chang and Lin, 2011). This method was employed to test our findings mentioned above of strong significant correlations between our measures and Private subscores. Due to our small number of observations (50) for this method, only the Private subscore was tested.

A linear SVM constructs an optimal linear hyperplane in the feature space, which classifies the data into two classes. We divided our participants into two classes: a ‘high Private self-consciousness’ class, and ‘low Private self-consciousness’ class. We determined that the mean Private SCS score among participants was 15.1, so each participant below the mean was labeled as ‘low Private self-consciousness’, and each above the mean was labelled as ‘high Private self-consciousness’. We used the results of the PLE, ACW, MI and eLORETA (both PCC and pACC) analyses as features, which resulted in five-dimensional data points. The SVM was trained on 30 random participants and then tested on the remaining 20 participants. It was trained to find the optimal model parameters in three successive search spaces, each with a 3-fold cross validation. First, we searched for the optimal model parameters (c and gamma) in a large search space, then the searching space was narrowed two more times into smaller and smaller spaces. When the optimal parameters are determined, the model is applied to the test set for classification. After classification, we extracted the feature weights to evaluate the importance of each feature for classification.

Results

Behavioral data

The Self-Consciousness Scale (SCS) yielded three subscores, one for Private, Public and Social (Fig 1). The distribution of the subscores were as follows: the mean of the Private subscore was 15.10, with the standard deviation 3.78 and the range from 7 to 25; the Public subscore had a mean of 10.52, standard deviation of 4.51 and range from 0 to 21; in the Social subscore, the mean was 7.60, the standard deviation of 3.56, and a range from 2 to 16.

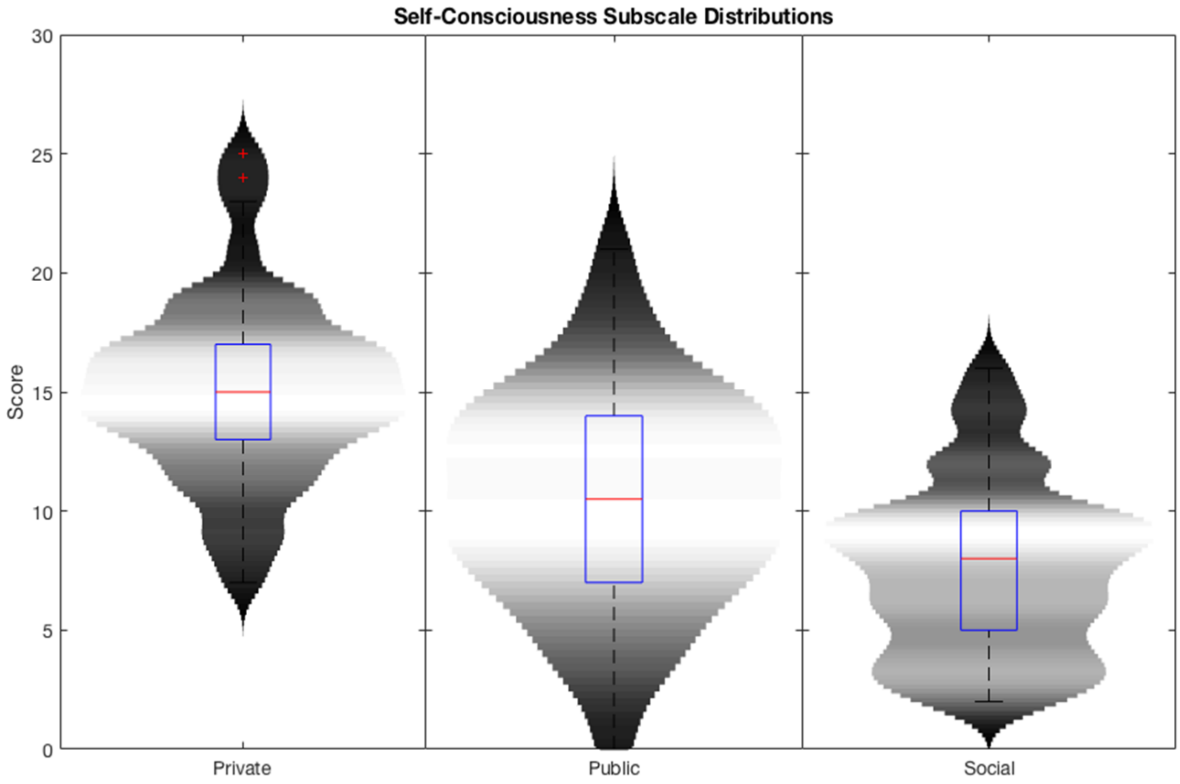

Figure 1*: Self-Consciousness subscale score distributions. Private (left), Public (center) and Social (right) are illustrated. The width of the plots denotes the number of observations, with wider areas having more observations. The horizontal line in the boxplots signifies the mean of the distributions, with crosses signifying outliers.*

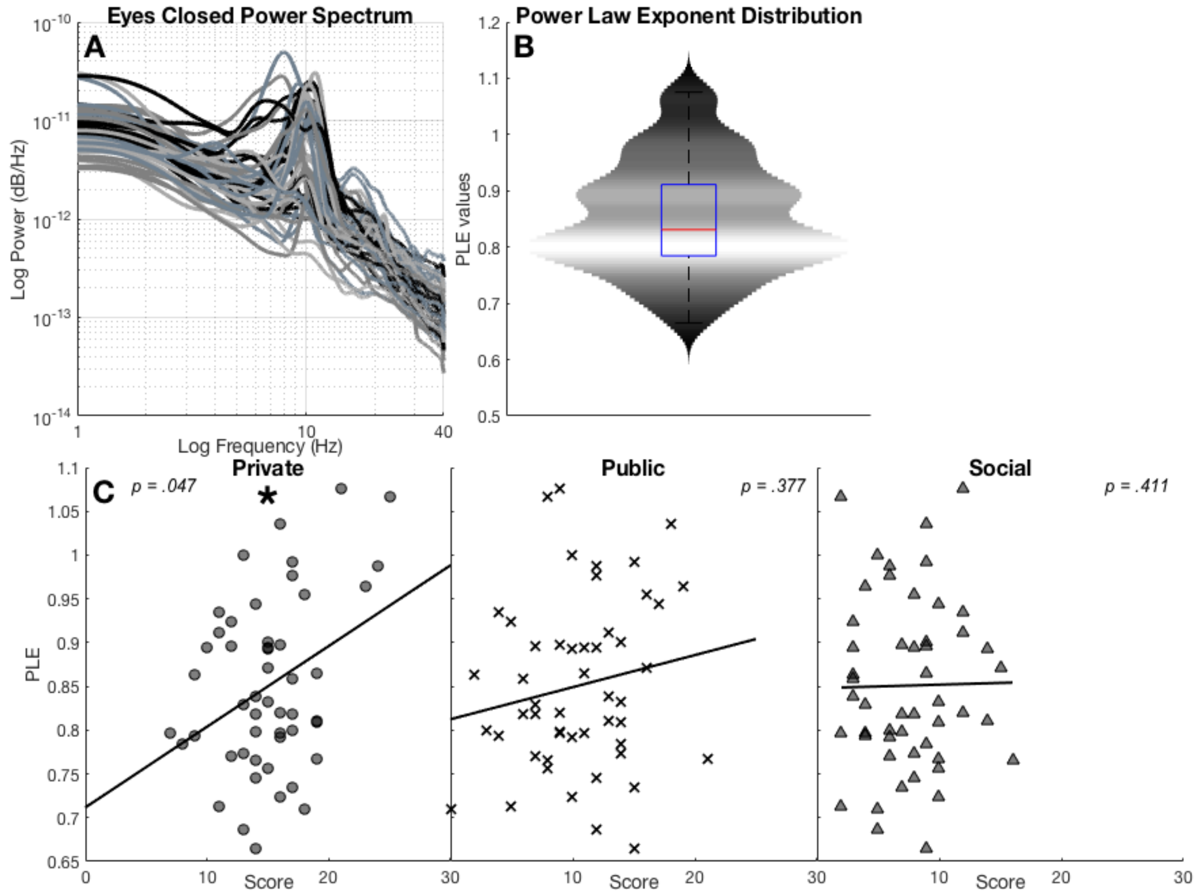

***Figure 2**: Power Law Exponent (PLE) distribution and correlation with SCS subscales. **A:** Log-log power spectrum of all participants for four minutes of eyes closed resting state, from which the PLE was calculated. Power spectrums are the mean of all channels. Alpha peak at roughly 10Hz is prominent since the resting state is eyes closed. Data was bandpass filtered from 1-40Hz. **B:** Distribution of PLE's for all participants from power spectrums seen in A. The width of the plots denotes the number of observations, with wider areas having more observations. The horizontal line in the boxplots signifies the mean of the distributions. **C:** One-tailed, bootstrapped partial correlations between PLE's and SCS subscale scores. The other two subscores were included as covariates in the partial correlations. Of the three subscales, only Private had a significant correlation with PLE's. Circle = Private, Cross = Public, Triangle = Social. P-values are FDR corrected.*

Power law exponent (PLE) and self-consciousness

The PLE was calculated based on the methods of He 2010, and Huang et al 2016 from the power spectrums of all 50 participants (Fig 2A). The distribution of the PLE values included a mean of 0.851, a standard deviation of 0.099, and a range of 0.665 to 1.076 (Fig 2B).

In one-tailed partial correlations with the SCS subscores (Fig 1), the Pearson correlation values for the PLE were the following: for the Private subscore, $r = 0.329$, $p = .047$; for the Public subscore, $r = 0.100$, $p = .377$; for the Social subscore, $r = -0.058$, $p = .411$ (Fig 2C).

To determine if the significant correlation between PLE and Private SCS was due to the power of any individual frequency band, we partially correlated the power - while controlling for the other two subscores - in delta (1-4Hz), theta (4-8Hz), alpha (8-13Hz), and beta (13-30Hz) with all three subscores.

The partial correlation results for the Private subscore were the following: in the delta band, $r = 0.198$, $p = .204$; in the theta band, $r = 0.072$, $p = .386$; in the alpha band, $r = 0.107$, $p = .377$; in the beta band, $r = 0.124$, $p = .477$. None of these partial correlations were found to be significant.

For the partial correlations with the Public subscore, the results were the following: in the delta band, $r = 0.100$, $p = .459$; in the theta band, $r = -0.092$, $p = .474$; in the alpha band, $r = 0.098$, $p = .491$; in the beta band, $r = -0.013$, $p = .420$.

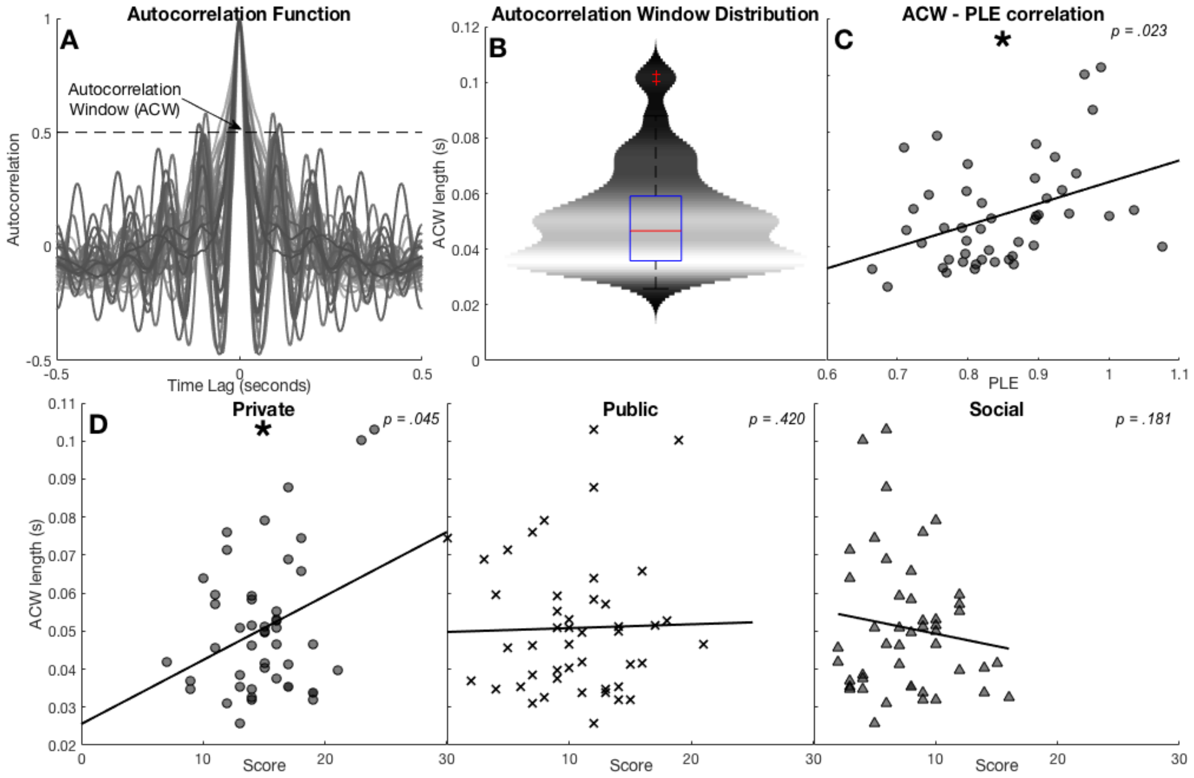

Figure 3**: Autocorrelation Window (ACW) distribution and correlation with SCS subscales.* ***A: *Autocorrelation function of all participants for four minutes of eyes closed resting state, from which the ACW (arrow) was calculated. The ACW was calculated by a 20 second window with 50% overlap and at lag of 0.5 seconds.* ***B:*** *Distribution of ACW's for all participants from Autocorrelation Function seen in A. The width of the plots denotes the number of observations, with wider areas having more observations. The horizontal line in the boxplots signifies the mean of the distributions, with crosses signifying outliers.* ***C:*** *One-tailed, bootstrapped correlation between ACW and PLE, which is significant (p-value stated).* ***D:*** *One-tailed, bootstrapped partial correlations between ACW's and SCS subscale scores. The other two subscores were included as covariates in the partial correlations. Of the three subscales, only Private had a significant correlation with ACW's. Circle = Private, Cross = Public, Triangle = Social. P-values are FDR corrected.*

Finally, with the Social subscore, the results were the following: in the delta band, *r* = -0.035, *p* = .386; in the theta band, *r* = -0.028, *p* = .386; in the alpha band, *r* = -0.137, *p* = .151; in the beta band, *r* = -0.146, *p* = .332.

Auto-correlation window (ACW) and self-consciousness

The ACW was calculated based on the methods of Honey 2012 from all EEG channels for the 50 participants. The ACW was determined from the autocorrelation function of each participant (Fig 3A). The distribution of the ACW values included a mean of 0.051, a standard deviation of 0.018, and a range of 0.026 to 0.103 (Fig 3B).

To determine the relationship of the ACW to the PLE, a one-tailed bootstrapped correlation was done which found a Pearson coefficient of $r = 0.394$, $p = .023$, 95% CI [.077, .622] (Fig 3C).

In one-tailed partial correlations with the SCS subscores (Fig 1), the correlation values for the ACW were the following: for the Private subscore, $r = 0.367$, $p = .045$; for the Public subscore, $r = -0.048$, $p = .420$; for the Social subscore, $r = -0.214$, $p = .181$ (Fig 3D).

Modulation index (MI) and self-consciousness

The MI was calculated based on the methods of Canolty 2006, Tort 2010, and Richter 2017 from all EEG channels for the 50 participants. It was also calculated in He et al, 2010 which examined scale-free brain activity and temporal structure, therefore this measure was calculated in addition to the PLE and ACW. The distribution of the MI values included a mean of 7.272, a standard deviation of 4.135, and a range from 1.151 to 18.963 (Fig 4A).

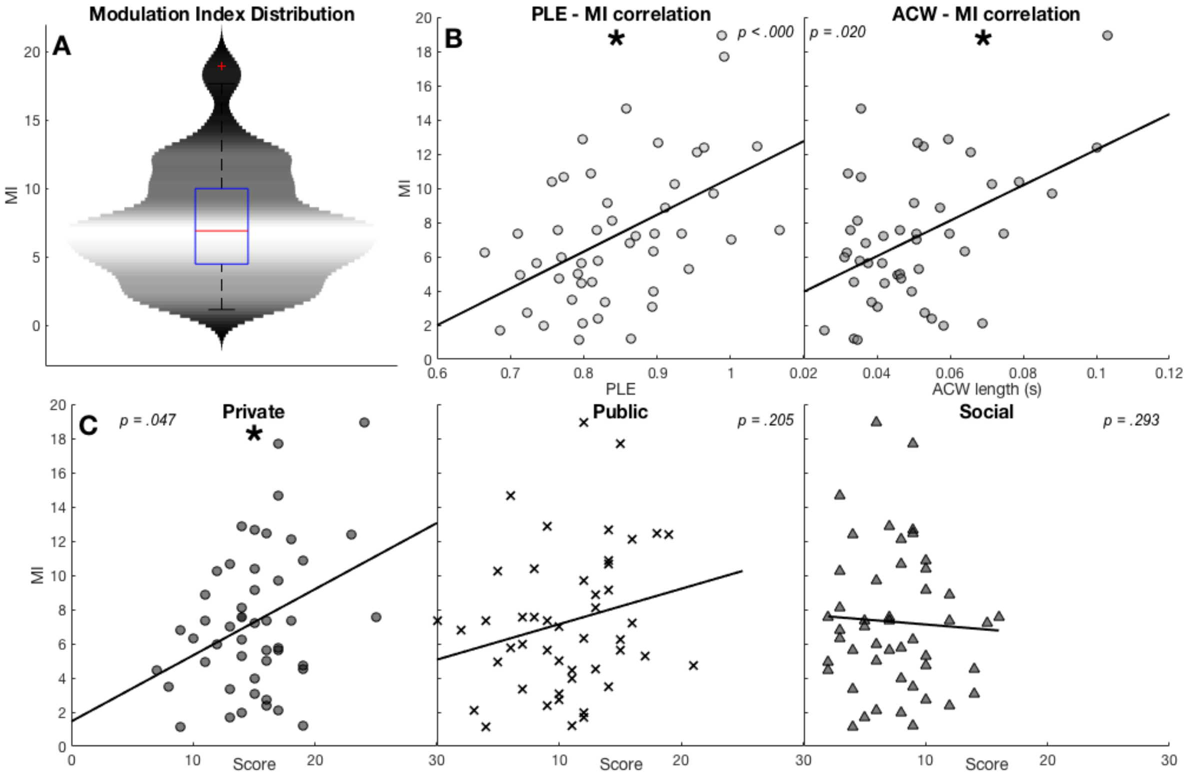

***Figure 4**: Modulation Index (MI) distribution and correlation with SCS subscales. **A:** Distribution of MI's for all participants calculated from four minutes of eyes closed resting state. The width of the plots denotes the number of observations, with wider areas having more observations. The horizontal line in the boxplots signifies the mean of the distributions, with cross signifying outlier. **B:** One-tailed, bootstrapped correlations between MI and PLE and ACW, both of which were significant (p-values stated). **C** One-tailed, bootstrapped partial correlations between MI's and SCS subscale scores. The other two subscores were included as covariates in the partial correlations. Of the three subscales, only Private had a significant correlation with MI's. Circle = Private, Cross = Public, Triangle = Social. P-values are FDR corrected.*

To determine the relationship of the MI to the PLE and ACW, two one-tailed correlations were done. The correlation between the MI and the PLE was found to be significant, with a Pearson correlation value of $r = 0.493$, $p = .000$, 95% CI [.292, .668] (Fig 4B).

The correlation between the MI and the ACW was also found to be significant, with a Pearson correlation value of $r = 0.474$, $p = .020$, 95% CI [.124, .717].

In one-tailed partial correlations with the SCS subscores (Fig 1), the correlation values for the MI were the following: for the Private subscore, $r = 0.312$, $p = .047$; for the Public subscore, $r = 0.192$, $p = .205$; for the Social subscore, $r = -0.147$, $p = .293$ (Fig 4C).

Private self-consciousness partial correlations controlling for other measures

From the results stated above, one further correlation was carried out. In this instance, however, the remaining two measures were also added as covariates. This would determine if the relationship between the Private subscore and the measure remained significant if the partial correlation included the other two measures as covariates, in addition to the public and social subscores.

Therefore, three one-tailed bootstrapped correlations were done. The first measured the partial correlation between the Private subscore and the ACW, while controlling for the public and social subscores, and the PLE and MI. The Pearson correlation value was r = .376, $p = .045$.

When the same correlations were performed with the PLE and MI – controlling for the MI and ACW, and the PLE and ACW, respectively – the correlations were no longer significant. The respective Pearson correlation values were r = -.166, $p = .279$, and r = .191, $p = .226$.

This indicates that only the ACW and Private subscore relationship was significant when the public and social subscores and the PLE and MI were controlled for.

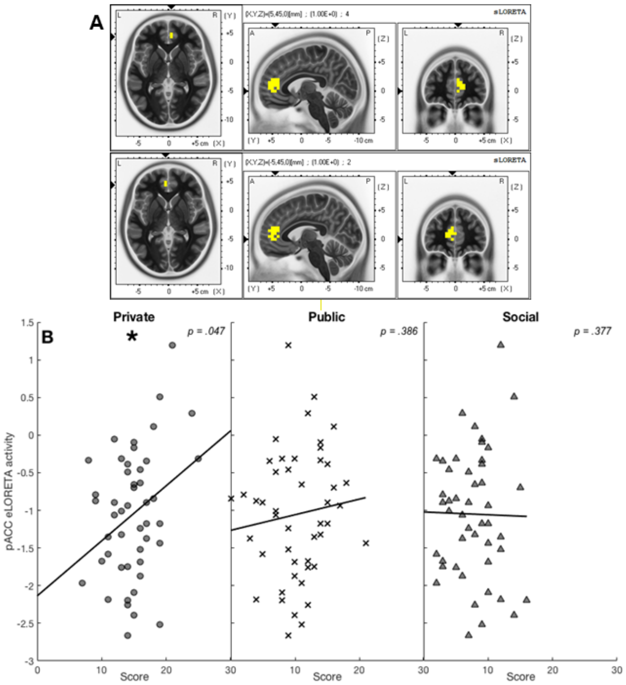

Figure 5: Perigenual Anterior Cingulate Cortex (pACC) eLORETA correlation with SCS subscales. ***A:*** *eLORETA localization of pACC (a cortical midline structure) based on MNI coordinates from a previous paper.* ***B:*** *One-tailed, bootstrapped partial correlations between pACC eLORETA values and SCS subscale scores. The other two subscores were included as covariates in the partial correlations. Of the three subscales, Private was just below the level of significance with the Bonferroni correction applied. Circle = Private, Cross = Public, Triangle = Social. P-values are FDR corrected.*

Tomography and self-consciousness

From the regions of interest for the Default Mode Network (DMN) in Huang 2016, we chose two regions to examine eLORETA activity in our data. These two regions were the pACC (Fig 5A) and the PCC (Fig 6A). With this activity, we did partial correlations with the SCS subscores (controlling for the other two subscores) to determine the relationship between self-consciousness and the activity in these two DMN areas. These regions were contrasted with two controls areas, not a part of the DMN, the cortex of the Dorsal Attention Network (DAN) and the cortex of the Motor Network (M1), and the whole cortex with no ROIs. In addition, these values of eLORETA activity were

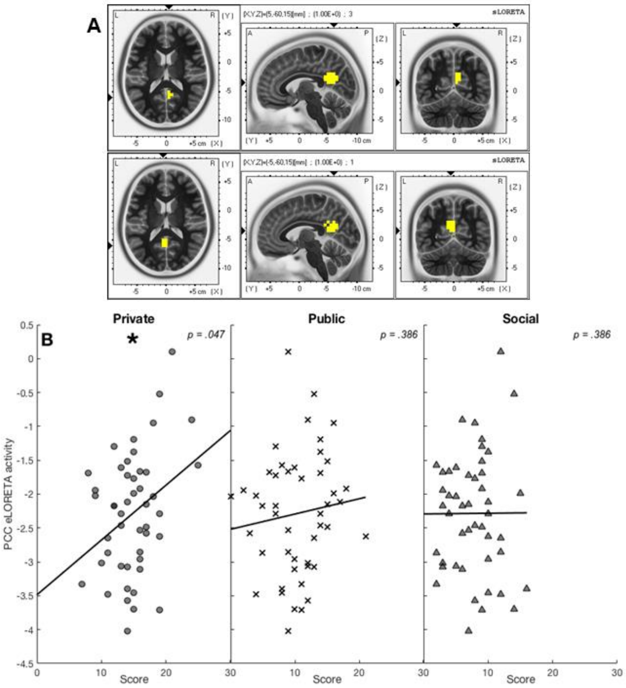

***Figure 6**: Posterior Cingulate Cortex (PCC) eLORETA correlation with SCS subscales. **A:** eLORETA localization of PCC (a cortical midline structure) based on MNI coordinates from a previous paper. **B:** One-tailed, bootstrapped partial correlations between PCC eLORETA values and SCS subscale scores. The other two subscores were included as covariates in the partial correlations. Of the three subscales, only Private had a significant correlation with PCC activity. Circle = Private, Cross = Public, Triangle = Social. P-values are FDR corrected.*

Table 1: Correlation between pACC and PCC eLORETA source current density and PLE, ACW, and MI

Correlation between eLORETA and:	pACC r* value	pACC p† value	PCC r* value	PCC p† value
PLE	0.339	0.023	0.332	0.023
ACW	0.331	0.047	0.322	0.047
MI	0.402	0.047	0.402	0.052

* Pearson *r* value for one-tailed bootstrapped (1000 samples) correlation
† FDR corrected for multiple comparisons

one-tail correlated with the other resting-state measures (PLE, ACW, MI) (Table 1). Significant *p*-values were found in correlations with all measures for both the pACC and PCC, but not in control regions.

In one-tailed partial correlations with the SCS subscores (Fig 1), the correlation values for the pACC eLORETA data were the following: for the Private subscore, *r* = 0.315, *p* = .047; for the Public subscore, *r* = 0.082, *p* = .386; for the Social subscore, *r* = -0.103, *p* = .377 (Fig 5B).

The Pearson correlation values for the PCC eLORETA data with the SCS subscores were the following: for the Private subscore, *r* = 0.327, *p* = .047; for the Public subscore, *r* = 0.076, *p* = .386; for the Social subscore, *r* = -0.083, *p* = .386 (Fig 6B).

Finally, the Pearson correlation values for the DAN eLORETA data with the SCS subscores were the following: for the Private subscore, *r* = 0.303, *p* = .234; for the Public subscore, *r* = 0.047, *p* = .969; for the Social subscore, *r* = -0.099, *p* = .969. The values for M1 eLORETA data with the SCS subscores were the following: for the Private subscore, *r* = 0.293, *p* = .234; for the Public subscore, *r* = 0.07, *p* = .969; for the Social subscore, *r* = -0.098, *p* = .969 (Fig 6B). As a last control measure, none of the correlations between the eLORETA activity in the whole cortex, with no ROI, and the SCS subscores were significant (*p* = .466, *p* = .302, *p* = .327, respectively).

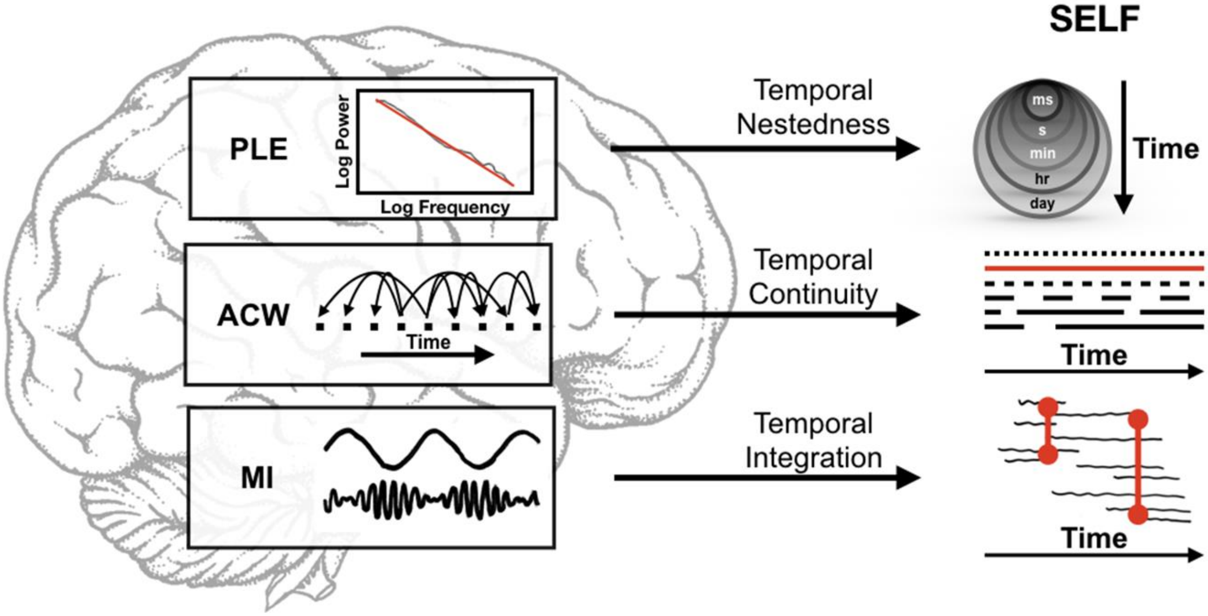

***Figure 7**: Schema of role and interaction of all three measures. PLE measures the temporal nestedness of frequencies, ACW measures the temporal continuity of frequencies, and MI measures the temporal integration of frequencies during the resting state.*

Support Vector Machine

The trained SVM could accurately distinguish ‘low Private self-consciousness’ and ‘high Private self-consciousness’ individuals from the test group. The trained SVM was tested using an independent testing set. It was 95% accurate, correctly labelling 19 of the 20 individuals in the test set. For this study, we were interested in the relative importance of each feature for classification, so we extracted the weights of each feature used to construct the separating hyperplane. The weight coefficient for the PLE was 0.37, for the ACW was 0.72, for the MI was 0.20 and for the eLORETA was 0.55 for the pACC and 0.56 for the PCC.

Discussion

We here investigated how the EEG-based temporal signature of the brain's spontaneous activity is related to self-consciousness. First, we demonstrated the positive relationship of temporal nestedness, as indexed by PLE, with Private self-consciousness. Second, the degree of the resting state's temporal continuity, as measured by ACW, correlated positively with both PLE and Private self-consciousness. Third, the temporal integration of the spontaneous activity, as measured by MI, was related to PLE and ACW as well as to Private self-consciousness. Finally, Private self-consciousness correlated positively with the EEG-source current density estimation from cortical midline structures, the pACC and PCC specifically. In both DMN regions, as the eLORETA current source density increased in participants, so did the Private subscore. This contrasts with the non-DMN control regions, which did not show a significant relationship with Private self-consciousness.

Our results strongly support our hypotheses. All measures of the resting state's temporal signature – PLE, ACW and MI - correlated positively with the degree of Private self-consciousness. In contrast, no such relationship was found for Public and Social self-consciousness. Moreover, our data show a significant relationship between two of the core cortical midline regions, pACC and PCC, and Private self-consciousness, but not the control regions. Together with our results on machine learning, our data strongly support the hypothesis that information about our self or self-representation is encoded and contained in the brain's resting state. This is known as rest-self containment. Most importantly, we find that such rest-self containment occurs on a temporal basis, specifically by the resting state's degree of temporal nestedness, temporal continuity, and temporal integration. As these three neuronal features find their direct analogues on the psychological level of the self, our results support a temporal basis of self as featured by the temporal signature of the brain's spontaneous activity (see also Northoff, 2017).

Taken together, our data shows that the temporal structure of the spontaneous activity encodes and contains information specifically about Private self-consciousness. This is further reinforced by our machine learning results, which shows that features extracted from the brain's spontaneous activity can be used to classify high versus low Private self-consciousness. Thus, the temporal signature of the brain's spontaneous activity can characterize our self and its self-consciousness. This suggests that temporal nestedness, continuity, and integration also hold on the psychological level of self, which therefore may be characterized in a temporal way (see Northoff 2016, 2017).

"Temporal nestedness" of spontaneous activity and self-consciousness

Our first main finding shows a positive relationship between the resting state's scale-free properties and Private self-consciousness. Higher values of the PLE were related to higher degrees of Private self-consciousness. Previous findings show a relation of scale-free properties with personality traits (Hahn et al., 2012; Lei et al., 2013) and self-consciousness (Huang et al., 2016) in the infraslow frequency domain (0.01 - 0.1Hz) as measured with fMRI. Our data shows an analogous relationship in the faster frequency domain (1 - 40Hz) of EEG. The higher the degree of the resting state's scale-free properties in these frequencies, the higher the degree of Private self-consciousness. Most interestingly, as in our previous fMRI study (Huang et al., 2016), this relationship only holds for Private, but not Public and Social dimensions of self-consciousness.

Scale-free properties describe the power relationship between slower and faster frequencies. As slower frequencies show stronger power than faster ones, the latter are temporally nested within the former – there is thus ‘temporal nestedness’ that indexes a fractal organisation between the different frequencies in the brain’s spontaneous activity (Linkenkaer-Hansen et al., 2001; He, 2011, 2014; Palva et al., 2013). Both our past (Huang et al., 2016) and present results suggests that such temporal nestedness on the neuronal level is closely related to our self through Private self-consciousness. This is further supported by the fact that the power of the single frequency ranges themselves did not predict Private self-consciousness. Hence, it is really the fractal organisation, and thus temporal nestedness, that encodes Private self-consciousness.

Psychologically, our self spans across different time ranges. Our self may exert impact on the level of seconds as, for instance, when impacting and modulating stimuli in terms of different degrees of self-relatedness (Northoff et al., 2006; Sui et al., 2012, 2013; Sui and Humphreys, 2015). This amounts to what has been described as “synchronic self” (Northoff, 2016b). At the same time, our self is also manifest in extremely long timescales and thus slower frequency ranges, as over days, weeks, and even years and decades. This thus reflects a ‘self-continuity’ as ‘diachronic self’ (Ersner-Hershfield et al., 2009b, 2009a; Northoff, 2017) which, following our data, may be traced to the temporal nestedness between the different frequencies in the brain’s spontaneous activity.

“Temporal continuity” of spontaneous activity and self-consciousness

Our second main finding concerns the relationship of the autocorrelation window (ACW) of our data to Private self-consciousness. What do these results mean? For that, we must go back to the neuronal level and consider what exactly the ACW measures. The ACW measures the degree of sameness of neural activity patterns across time when correlating the different time points with each other. As the slower frequencies, due to their long cycle duration and strong power, shape the ACW more strongly that shorter and less powered faster frequencies (Honey et al., 2012), one would expect positive correlation between scale-free properties such as the PLE, and the ACW. This is exactly what our results revealed.

Longer ACW indicates that neuronal activity remains the same over time. Hence, ACW can be said to measure the degree of “temporal continuity” of the brain’s spontaneous activity. Most importantly, our results show that such temporal continuity on the neuronal level is related to our self, specifically Private self-consciousness; the higher the degree of temporal continuity on the neuronal level, the higher the degree of Private self-consciousness. In contrast, no such correlation was observed for Public and Social self-consciousness. Hence, temporal continuity on the neuronal level may be directly related to self on the psychological level. This relationship is embodied by our machine learning model, in which the ACW was the most heavily weighted feature for classification. This reinforces the special relationship of the brain’s temporal continuity to self-consciousness.

The relationship between temporal continuity on the neuronal level and self-consciousness on the psychological level is of interest given that psychologically the self can indeed be characterized by its continuous nature, specifically self-continuity resulting in personal identity (Northoff, 2017). The self has been demonstrated to delay reward choice more strongly than non-self (Ersner-Hershfield et al., 2009b) – the self thus appears to infuse temporal delay with temporal continuity into psychological functions such as reward. This is even more interesting given that the ACW on the cellular level has been related to the degree to which monkeys can delay reward delivery (Murray et al., 2014). Temporal continuity, on both the neuronal and psychological levels, thus seem to provide the “glue”, or “common currency”, between the brain and the self.

“Temporal integration” of spontaneous activity and self-consciousness

Our third main finding consists in the relationship between cross-frequency coupling (as indexed by MI) and Private self-consciousness. As in the other measures, we observed a positive correlation between MI and Private self-consciousness. No such relation was observed for Public and Social dimensions of self.

Cross-frequency coupling describes the relation between slower and faster frequencies; the slower frequency couples to the faster frequency (Aru et al., 2015; Hyafil et al., 2015). Interestingly, we observed the degree of CFC to be related to both PLE and ACW. Higher degrees of CFC were directly related to stronger PLE and longer ACW. Given that all three measures are strongly driven by the slower frequencies as featured by long cycle duration, one would have expected their correlation. This is also in line with the findings by He (2010) who observed a close relation between scale-free properties and CFC (as measured with MI) in ECoG. Our results replicate and extend these findings by showing that CFC correlates not only with PLE, but also with ACW.

Psychologically, the self has been associated with integration in various functions. The self promotes integration of sensory (Sui et al., 2012, 2013), motor (Frings, C. &

Wentura, 2014), reward (Sui et al., 2013; Sui, 2016), cognitive, specifically attention (Sui et al., 2013) and decision making (Nakao et al., 2012, 2013a), and emotional (Northoff et al., 2009) functions. Therefore, Sui and Humphreys (2015) characterized the self by integration, therefore self-integration, where the self provides some sort of "glue" on the psychological level.

How does the integrative function of self on the psychological level stand in relation to temporal integration on the neuronal level as in CFC? Integration on the psychological level is possible only by integrating the different time scales of the various functions and their respective contents. Hence, integration on the psychological level is possible only if integrating different time scales and their respective frequencies. We now assume that such temporal integration on the psychological level is mediated by temporal integration on the neuronal level, which in turn is mediated by CFC.

Based on the MI, which measures CFC, we assume that the integrative function of self allows one to relate short, fast frequency stimuli (as in the beta and gamma frequency range) to the brain's ongoing spontaneous activity, with its stronger power in the slower frequency ranges of delta, theta, and possibly even the infraslow ranges (0.01 to 0.1Hz). Specifically, one would hypothesize that the fast frequency stimuli are processed by equally fast frequencies whose amplitude, as evoked during task-evoked activity, may then be coupled to, and thus integrated with, the spontaneous activity's long phase durations of the slower frequencies. This would produce slow-fast phase-amplitude coupling. We consecutively hypothesize that such coupling from the slower frequencies' phase to the faster frequencies' amplitude - crossing between spontaneous and task-evoked activity - may signify the integrative function of self as described by Sui and Humphreys (Sui and Humphreys, 2015). However, to demonstrate that, future studies are needed which link self-integration on the psychological level to phase-amplitude coupling on the neuronal level.

Limitations

We here tested only for resting state; we did not include an explicit self-related task in our study. Future studies may therefore want to test how the applied measures of PLE, ACW, and MI are modulated during task-evoked activity and how that is related to Private self-consciousness.

Next, we are not able to disentangle self and consciousness. Previous investigations suggest that the self may already be processed unconsciously, for example during the absence of consciousness (Qin and Northoff, 2011; Huang et al., 2014). Future studies may therefore dissociate self and consciousness and investigate which is related to the various measures of the temporo-spatial signature.

Thirdly, we were unable to locate exactly the temporal measures in specific regions of the brain due to the spatial limitations of EEG. Our data does however support the involvement of cortical midline structures, such as the pACC and PCC, as their eLORETA-based activity correlated only with Private self-consciousness.

Finally, our support vector machine analysis employed a rather small amount of training data. As this analysis was merely to supplement our main findings, we did not view this as a major issue.

Conclusion

We investigated the temporal signature of the brain's spontaneous activity with EEG and linked that to self-consciousness. Our findings show that specifically Private self-consciousness is positively related to neuronal measures of temporal nestedness through PLE, temporal continuity through ACW, and temporal integration through CFC/MI. Together with our results from machine learning, these findings suggest that the self is encoded (or represented) in the brain's spontaneous activity in a temporal way. The temporal signature of the brain's spontaneous activity may thus encode or represent self-related information in a temporal way. Though not demonstrated here explicitly, our data suggest that the temporal features of the brain's spontaneous activity - temporal nestedness, continuity, and integration - translate into corresponding temporal features on the psychological level. Temporal features may thus provide the "common currency" between brain and self such that the latter can then be characterized primarily in a temporal way.

Acknowledgments

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The authors state no known conflicts of interest.

Discussion

The central goal of this project was to determine markers of individualization at the behavioural, the neuronal, and the mental levels. This was achieved through the validation of the consequential threshold for moral dilemmas as a marker of behavioural individualization first. Once this was confirmed, the disambiguation of the neuronal markers of individualization were done. They were found to be alpha activity, specifically during the time interval of the LPP, TTV within the alpha and beta frequency bands, prestimulus Lempel-Ziv complexity, and the scale-free measures of spontaneous resting state activity, the power law exponent (PLE) and autocorrelation window (ACW) in particular. Finally, the marker of mental individualization was found to be the self through the Private subscore of the SCS.

Inter-subject variability on the behavioural level and task-evoked activity - threshold variability and the Late Positive Potential

Behavioural findings

In the behavioral session, the consequential threshold was determined. The distribution of thresholds showed variability across participants, with the distribution negatively skewed towards the more consequential thresholds. The largest group had the most consequential threshold, 5:7, though the numbers were roughly even in the other, less consequential thresholds. This is consistent with previous studies, though these studies have looked at the effect of intoxication (Duke, 2015), psychopathy (Aharoni, 2011; Koenigs, 2012), or personal versus impersonal scenarios (Wang, 2014) on level of consequential responses.

The study most closely related showed very similar results (Bonnefon, 2016), with variability across participants, but with agreement as to the action taken increasing as the number of people saved also increased. Since examining variability between individuals was our central research question, the distribution of thresholds validated our paradigm.

Concerning reaction times, it was determined that the moral trials had significantly longer reaction times than control. Previous studies have shown higher reaction times in personal dilemmas compared to impersonal dilemmas (Wang, 2014), and higher reaction times when family members are involved in the personal scenario compared to the involvement of strangers (Chen, 2009). This shows a significant effect of condition on reaction time, which we extended here to a significant effect of proximity to threshold as well; the near threshold stimuli had significantly longer reaction times. That suggests a more demanding task and higher conflict, which is consistent with the literature related to internally guided decision making (Nakao et al., 2012) and is consistent with the results found when family members were involved in the personal dilemmas (Chen, 2009).

The threshold distribution itself had a significant effect on reaction time, with the more consequential thresholds (5:7, 4:8, 3:9) having longer reaction times than the less consequential thresholds (1:11, 2:10). Since our research questions concerned variability in consequentialism and interindividual differences - both of which are measured by the varying thresholds - the behavioural results provide the foundation on which to continue with these questions when assessing our neural data.

Neural findings

As said in the literature (Hajcak, 2009; Ferrari, 2008; Weinberg, 2012), this study indicates that in both the early and late time windows, late positive potential (LPP) activity was driven by motivated attentional processing (Gable, 2013). Our moral task may have required more sustained attentional resources, which is why the difference in activity was still significant at the late time window, but it was higher in this later interval. The longer reaction time in the moral condition, as well as the correlations between the later activity and the emotion scores, show that in the control condition, the peak activity was reached earlier than in the moral condition, which had a longer, more sustained peak.

Subjectively perceived emotion scores, to which the participants responded after their EEG session, significantly correlated with moral individualized stimuli activity in the LPP late time intervals. This supports our previous findings that interindividual differences in activity is isolated to the later time intervals and only is related to interindividual differences, as can be measured by variable reaction times, in the LPP late time interval.

Our data show that, though early components do show differences between conditions, variability in frequency band power between participants and emotional assessments of the scenarios develop longer after the stimulus onset, specifically between 1000 and 2000ms. This was shown by the alpha power in this late time interval, and their significant relationship to both reaction times and emotion scores. Despite these findings late in the epoch, we found that ITC very early also differed based on condition and proximity to threshold, which itself showed a significant correlation with the emotion scores. Together, phase in the early part of the epoch relates to moral reasoning and interindividual emotional assessments of the moral scenarios, and alpha power and individual differences related to moral reasoning arise much later in the epoch, mostly after 1000ms.

Therefore, the late ERP component showed greatest differences related to consequentialist reasoning, though there were early differences in alpha, as well as the largest differences between participants. Findings related to ERSP and ITC were specific to the moral condition, as were the significant correlations between these neural measures and the behavioural measures. Phase coherence early after stimulus onset and alpha activity long after stimulus onset were found to be the best markers of interindividual differences as they correlated significantly with behavioural measures, such as reaction time and perceived emotional distress. Activity during the time interval of the LPP appears to be when the later, more individual influences of emotion and personality manifested.

The behavioural findings of variability across thresholds and reaction times validated our paradigm and allowed us to continue examining interindividual differences related to variability quenching in article two. In addition, the findings here of significant differences in the ERSP in the alpha and beta bands suggested to us that the TTV should be investigated in individual frequency bands, as well as the broadband. The alpha findings which correlated with the behavioural measures in article one indicated to us that the sensitivity of alpha power to stimulus onset may act as a specific marker of individual neural activity. This idea was important for article two as examining TTV quenching as an individual neural marker was one of our aims, and focusing on the alpha band, as well as the beta band, as a possible candidate provided us with one of our hypotheses.

Interindividual variability is indexed by alpha activity as trait biomarker

Alpha in EEG

As the first frequency band described in EEG, alpha activity has been much studied and reviewed (Klimesch et al., 2006, 2007, 2011; Fellinger et al., 2011; Hanslmayr et al., 2011; Klimesch, 2011; Başar and Güntekin, 2012; Bazanova and Vernon, 2014; Bröltzner et al., 2014; Gruber et al., 2014; Mierau et al., 2017). One dominant hypothesis regarding the role of alpha has been related to inhibition, specifically the inhibition-timing hypothesis (Klimesch et al., 2007; Klimesch, 2012). This hypothesis theorizes that inhibition is an active process which facilitates the processing of information through increasing the signal to noise ratio (SNR) (Klimesch, 2012). It suggests that inhibition allows for the silencing of brain areas irrelevant to the task at hand, while the release from inhibition allows for excitation of brain areas required for it; this may be how alpha inhibition allows for the decrease of the noise and the amplification of the signal (Klimesch, 2012; Shen, 2011; Yizhar, 2011).

Prior to stimulus onset, alpha synchronization - an increase in alpha amplitude - is theorized to relate to active inhibitory control, while alpha event-related desynchronization - a decrease in alpha amplitude after a stimulus is presented - is related to a release from inhibition (Başar and Güntekin, 2012; Klimesch, 2012). This attentional 'filter' as it is described by Klimesch, has been thought to be 'paced' by the alpha oscillations; the oscillations become 'entrained' by the frequency of the sensory stimulation (Klimesch, 2012). In addition to this theory, there has been previous evidence that alpha acts as a gating mechanism in sensory coding for visual stimuli (Zumer, 2014), and for gating inhibition generally (Jensen, 2010).

Alpha peak frequency and alpha power

It was recently suggested that alpha peak frequency (APF) variability is a self-regulated and independently tuned mechanism that can be recorded at the scalp, but reflects activity at the neural population level and adjusts to task demands (Mierau et al., 2017). Many tasks including cognitive (Jann et al., 2010; Haegens et al., 2014; Maurer et al., 2015), motor (Angelakis et al., 2004), physical (Nir et al., 2010; Hulsdunker et al., 2016; Gutmann et al., 2018), pharmacological (Lindgren et al., 1999; Bchir et al., 2006), emotional (Kostyunina and Kulikov, 1996), and related to level of consciousness (Lechinger et al., 2013, 2015; Purdon et al., 2015) have been shown to modulate APF in individuals.

Studies have shown that external inputs related to a task cause neural populations to become increasingly linear (Sutherland et al., 2009; Tuckwell et al., 2009). With respect to oscillations, this increasing linearization amounts to a change in peak frequency. In the resting state, neuronal firing rates are lower than during tasks (Mierau et al., 2017), and it is thought that this is seen in lower APF. With the onset of a task, however, neural spiking in a population will rise. Computational studies have shown that this increased firing rate will bring about a change in the system's response through feedback loops, and this will affect the resulting oscillations and the APF (Mierau et al., 2017).

Therefore, these findings show that the input to the system has a large influence on its emerging oscillations and this can be seen in shifts in peak frequency (Mierau et al., 2017). A further support to this is found in studies which suggest that alpha power can be a transient index of cortical excitability (Romei et al., 2008a, 2008b; Lange et al., 2014), and broadly that indicators of alpha activity can serve as a characteristic of an individual's visual system in sensory perception (Cecere et al., 2015). Furthermore, it has been suggested that it is alpha oscillations which gate visual perception through changes in inhibition and excitation (Klimesch et al., 2007; Mathewson et al., 2009; Romei et al., 2012).

Other studies have proposed that alpha activity may control the sampling rate of the environment by cortical neurons (Cecere et al., 2015; Samaha and Postle, 2015). This is supported by evidence that prestimulus alpha power predicts the ability of the individual to adjust during a trial at the behavioural level (Horschig et al., 2014). These findings suggest that posterior alpha power is modulated by the participant integrating statistical knowledge about the environment, therefore exerting top-down control (Horschig et al., 2014).

Together, this evidence indicates that alpha activity changes across tasks within an individual are a result of the state they are in or task they are doing. Differences between individuals, on the other hand, are due partly to genetics (Posthuma et al., 2001; van Beijsterveldt and van Baal, 2002) and brain structure (Valdes-Sosa et al., 2009). Rest alpha activity and activity in response to a task are thought to be influenced by genetics through the balance of excitation and inhibition in the brain and their influence on cortical circuit development (Isaacson and Scanziani, 2011; Turrigiano, 2011; Mierau et al., 2017).

Other factors which influence the development of these cortical networks, specifically during sensitive periods, are likely to influence the excitation/inhibition balance in the individual (Turrigiano, 2011). It has been shown that negative experiences during childhood have a significant effect on cortical network activity (Duncan et al., 2015; Watt et al., 2017), so perhaps this could influence the development of structure of the individual's brain (Northoff and Stanghellini, 2016).

Alpha activity and its response to a stimulus, and neural variability prior to stimulus onset, are both thought to be determined by activity in cortical networks. The structure and function of these cortical networks are shaped first by genetics, probably in the form of the balance between excitation and inhibition (Ferri et al., 2017), then later during early childhood (Hensch, 2005) by the environment which further shapes cortical activity at rest (Duncan et al., 2015; Watt et al., 2017).

Alpha in our findings

From the extensive literature on alpha activity generally, our findings in the first moral study and the second TTV study are not surprising.

Despite there being, to our knowledge, only one study which investigates alpha power in a moral context (Petras et al., 2016), they found that alpha power was significantly lower in the moral condition compared to the non-moral condition. In the first moral paradigm study, our results show that in the LPP time intervals there were significant differences in alpha power between stimuli near the threshold compared to far from the threshold, only in the moral condition.

Several studies have shown that alpha power is influenced by attention and arousal (Shaw, 1996; Cantero et al., 1999; Keil et al., 2001; Simons et al., 2003), with an inverse correlation. This therefore suggests that there were attention and arousal differences in the moral condition, with more of a decrease in the stimuli around the threshold than in those far from the threshold. These near threshold stimuli were also those individualized, and as we saw in the second TTV study, in the alpha band there was a significant difference between groups of stimuli in the TTV index.

It has been shown that internally-guided decision-making[4], of which the moral paradigm is an example, has been related to differences in activity in the alpha frequency band (Bai et al., 2016). Questions of preference appear to have a differential impact on activity in the alpha band (Nakao et al., 2013a; Bai et al., 2016), which is consistent with our findings between individualized and shared stimuli in the first and second study. In addition, the differences found only in the moral condition show that there is an interaction between stimulus and condition, both in prestimulus and poststimulus induced activity. In the moral condition, it appears that the nature of the stimulus (individualized or shared) was relevant for the task, which was not the case in the control condition. Therefore, we suggest that the individuality of the stimulus interacted with the context (moral condition) and produced differences in the alpha band between stimuli. This context-dependent factor was absent in the control condition, therefore no differences in alpha band were seen.

Future questions related to these findings are the following. These ‘intrinsic mechanisms’ of cortical activity (Arazi et al., 2017b) are stable in adulthood, however at what point is this stability reached? In addition, though neural variability has influence on behavioural outcomes (Xue et al., 2010; Schurger et al., 2012, 2015; He, 2013; He and Zempel, 2013; Arazi et al., 2017a), is there an ‘optimal’ range of neural variability

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[4] Internally guided - no correct answer is available.

Externally guided - one predictable answer is available. (Nakao et al., 2012)

(He and Zempel, 2013), outside of which psychopathological symptoms become likely (Dinstein et al., 2012; Yang et al., 2014a; Gonen-Yaacovi et al., 2016)? These questions, along with a stronger link to genetic foundations and early life environmental influences, must be addressed in future studies.

Neuronal Variability as index of neural individuality?

Information and attractors

We are provided with a continuous time series of information from the environment through our sensory system. The online[5] analysis of incoming information, it has been shown, is vital to an organism's survival; if they fail to perform quick and instructive analyses as information arrives and react in accordance, they may not survive (Gros, 2015).

First developed by Shannon, Information Theory was conceived of as a way to measure the transfer of information through a message in a noisy system (Shannon, 1948). As stated above, the processing and integration of information is vital to the survival of an organism, and in neuroscience, information transfer occurs via spiking of individual neurons (Deco and Hugues, 2012; Naud and Sprekeler, 2018), oscillations (Buzsáki and Draguhn, 2004; Sauseng and Klimesch, 2008; Honey et al., 2012; Pascual-Marqui et al., 2014; Foster et al., 2016), and interaction of frequency bands (Sauseng et al., 2007; Canolty and Knight, 2010; Lisman and Jensen, 2013).

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[5] Online analysis is performed during recording – 'on the fly' – while offline analysis is performed on a timeseries after the recording is complete (Gros, 2015).

The influences on vehicles of information transfer has been stated as genetics (Turrigiano, 2011) and early environmental factors (Hensch, 2005; Duncan et al., 2015; Watt et al., 2017) as they shape cortical networks which give rise to neural variability and oscillations. This electrophysiological activity can be measured through information theory complexity and scale-free measures.

In their 2012 study, Deco and Hugues asked why cortical circuits show high variability across trials and then why does this decrease after stimulus onset (Deco and Hugues, 2012). In a computational neural network model, they were able to show that this decrease in variability can be an effect of the network itself. They found excitation by an external input stabilized one attractor in a multi-attractor system. This stabilization meant a reduction in the possible transitions between available attractors – during spontaneous activity, multiple configurations arise between the attractors in the system (Deco and Hugues, 2012; Huang et al., 2018). The stabilization of the one attractor reduced the possible attractors available (Huang et al., 2018). This reduced available transitions and led to a decrease in neural variability (Deco and Hugues, 2012; Huang et al., 2018).

They also showed that stimulus onset lead to an increase in the SNR of the spike count (an increase of the consistency of the spike train firing) (Deco and Hugues, 2012), as measured by the Fano factor (Rajdl and Lansky, 2014), and suggested that this showed ‘improved encoding of the external signal’ (Deco and Hugues, 2012). Though these important findings were measured in a computational model, a recent TTV study in humans using fMRI proposed this as the possible mechanism underlying neural variability quenching after stimulus onset (Huang et al., 2018).

Trial-to-trial variability as marker of neural variability

The magnitude of neural variability is a stable individual characteristic; it is consistent over time, across tasks, in different modalities and under various cognitive demands (Arazi et al., 2017b). It has also been shown that the magnitude of neural variability changed very little in response to task demands, which further supports the idea of TTV as a marker of individual brain activity (Arazi et al., 2017b). What factors shape this neural variability, then, and how does this, or its suppression through quenching, constrain the behaviour of the individual?

It has previously been proposed that neural variability quenching is partly a function of attention (Deco and Hugues, 2012; He, 2013; Gao et al., 2018). When this was examined explicitly, it was found that in participants with ADHD, variability was higher generally, including prior to stimulus onset and trials in which no stimulus appeared (Gonen-Yaacovi et al., 2016). This finding therefore suggests that the influence of attention in TTV may be as a trait feature - ongoing characteristic of the individual brain - rather than a state feature - attention related to the stimulus (Aston-Jones and Cohen, 2005; Mitchell et al., 2007, 2009; Sakata et al., 2008; Cohen and Maunsell, 2009; Garrett et al., 2015).

Genetics then, and early environmental factors are the suggested sources of individual neural variability (Arazi et al., 2017b, 2017a), as they were for alpha peak frequency. Both highly individual factors, their strong influence on neural variability and alpha activity support these measures as markers of brain activity specific to the individual.

TTV findings in our studies

As mentioned above, TTV has been shown to be stable within participants and across tasks, so therefore may act as a trait marker of individual brain activity (Arazi et al., 2017b). If true, we hypothesized that poststimulus TTV activity would be different to stimuli individualized to the participant than stimuli not individualized.

This was found in the alpha and beta bands and was further supported by the significant correlations between their TTV indices and reaction time and prestimulus LZC. Finally, the threshold, when divided into three roughly equal groups, had a significant effect on the individualized TTV index in the alpha band. The significant relationship between these behavioural measures – as was seen in the LPP alpha activity and ITC of the first study – and the neural measures supports the hypothesis that the TTV index in the alpha and beta bands serves as a marker of individual brain activity. Finally, the inclusion of the LZC measure, specifically in the prestimulus period, provided evidence that the complexity of the spontaneous activity might also serve as a marker of neural individuality. Much further study of this and its specificity, however, are required.

Mental and neuronal variability – Self and the brain’s spontaneous activity

Self and spontaneous activity’s temporal structure

As was stated previously, some information specific to the private or individual self is encoded in the brains resting state spontaneous activity (Huang et al., 2016). As measures of the resting states temporal structure correlated with the private SCS scores, it may be that the rest-self overlap in certain CMS areas are mediated by the temporal structure of the brains resting state (Huang et al., 2016). As shown by the moral CMS study, these areas also overlap with moral processing, specifically in personal moral dilemmas (Han et al., 2016).

We found that our three measures of resting state activity – PLE, ACW and MI – correlated with the private SCS scores, as did the eLORETA activity from the pACC and PCC. These findings were able to replicate, though in a much higher frequency range, the previous results of the similar fMRI study (Huang et al., 2016), which suggest that this relationship exists on a continuum of frequency ranges, from the very slow in the fMRI range, to the much faster in the EEG range.

It has been shown that during the resting state activity in the DMN increases (Raichle et al., 2001; Raichle, 2015). The same increased activity in the CMS was seen during moral dilemma tasks (Han et al., 2016). The next question to ask, therefore, is whether the resting state, specifically activity in the DMN, contains information relevant to moral decision-making in the individual. In addition, it must be determined how moral processing, which has been shown to have interindividual differences, is related to private self-consciousness. Future work must investigate such a connection.

In our study, we found that higher values of the PLE were related to higher degrees of Private self-consciousness only, not Public or Social. Such a relationship has been shown previously in the infraslow frequency range of fMRI (Hahn et al., 2012; Lei et al., 2013; Huang et al., 2016), however we were able to show this, for the first time, in the higher frequency range of EEG.

An entity is scale-free when it has no characteristic scale, and a scale-free entity can exist in either the temporal or spatial domain (He et al., 2010; He, 2014). In EEG activity, the log-log transformed power spectrum shows that lower frequencies have higher power than higher frequencies, which has suggested that faster frequencies are ‘nested’ within the slower ones (Linkenkaer-Hansen et al., 2001; He, 2011, 2014; Palva et al., 2013). This temporal nestedness can serve as an indicator of the scale-free organization between different frequencies in the EEG spectrum with the PLE as its measurement.

As our results correlated with the PLE only in the Private subscore, and since the power of each frequency band failed to correlate, this organization of the frequencies contains some information related to private self-consciousness. The ‘synchronic self’ functions at the temporal scale of seconds (Northoff et al., 2006; Sui et al., 2012, 2013; Sui and Humphreys, 2015) while the ‘diachronic self’ functions on a larger scale of days and weeks (Ersner-Hershfield et al., 2009b, 2009a; Northoff, 2017). Our results, as well as the previous ones in fMRI (Hahn et al., 2012; Lei et al., 2013; Huang et al., 2016), may link the temporal nested of the self and that of the spontaneous activity of the brain.

The ACW findings show that participants with a longer ACW have higher private self-consciousness as indexed by the Private SCS subscore. As the ACW is more strongly shaped by the slower frequencies (Honey et al., 2012) which have longer cycles, participants with a longer ACW have longer temporal continuity in spontaneous activity. This finding that longer temporal continuity relates to more private self-consciousness relates to the self at the psychological level by two studies. The self has been implicated in delaying reward choice in both humans (Ersner-Hershfield et al., 2009b) and non-human primates (Murray et al., 2014). Future studies must further test this relationship.

As with the previous measures described, CFC relates the various frequencies together by measuring the amount of coupling between the slower and faster frequencies (Aru et al., 2015; Hyafil et al., 2015). The relationship between CFC and the Private subscore was the same as seen with the PLE and ACW. In previous studies, the self has been shown to modulate the integration of many psychological factors (Northoff et al., 2009; Nakao et al., 2012; Sui et al., 2012; Nakao et al., 2013a; Sui et al., 2013; Frings, C. & Wentura, 2014; Sui and Humphreys, 2015, 2017). The link from integration of the self to the CFC may occur through phase-amplitude coupling (PAC) which measures coupling between the phase of the slower nested frequency and the amplitude of the faster nesting frequency (Tort et al., 2010; Bergmann and Born, 2018). As described in a 2015 article (Sui and Humphreys, 2015), the self may act as a binding agent to integrate aspects of cognitive and perceptual tasks. It may be that CFC through PAC measures this, however further studies must be conducted to examine it.

Conclusion

The need for individual neural markers has been expressed in both basic and clinical neuroscience (Braver et al., 2010; Reineberg et al., 2015; Friedman and Miyake, 2016; Jang et al., 2017; Seghier and Price, 2018). Specifically, in the clinical domain interindividual variability between patients may shed light on why symptoms within a given illness vary from patient to patient.

To address this, we here designed a novel behavioural paradigm in which to test several measures as possible markers of neural individuality. The individualized paradigm for consequentialist moral dilemmas was validated, showing variability across participants in thresholds and reaction times. Next, task-induced activity changes during the time interval of the late positive potential (LPP) in alpha power, along with phase coherence early in the trial, correlated with reaction times and scores of subjective emotional distress. From these findings in study one, in study we measured TTV and found that the TTV index in the alpha and beta bands correlated with reaction time and prestimulus LZC. These findings, again in the alpha and beta bands, support alpha power during the LPP, variability quenching in these bands, and early ITC as markers of neural individuality.

Finally, measures of scale-free activity in the resting state, along with others, and self-consciousness scale subscores as indices of the self were investigated. It was found that the PLE, ACW, MI and eLORETA activity in two DMN area correlated significantly with the Private subscore only. These findings indicate that these resting state measures, along with activity in the DMN, may serve as markers of neural individuality in the brain’s spontaneous activity.

In conclusion, the threshold and reaction times of the consequential moral dilemma provided behavioural measures of individuality; alpha activity late in the trial and phase activity early in the trial provided stimulus induced neural markers of individuality; trial-to-trial variability in the alpha and beta bands and prestimulus Lempel-Ziv complexity provided additional neural markers of individual brain activity; and finally the power law exponent, autocorrelation window, and modulation index during resting state activity provided measures of neural individuality in the brains spontaneous activity.

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