

# Empathy Dynamics: A Neuroscientific Perspective

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Niloufar Zebarjadi



# Empathy Dynamics: A Neuroscientific Perspective

**Niloufar Zebarjadi**

A doctoral dissertation completed for the degree of Doctor of Science (Technology) to be defended, with the permission of the Aalto University School of Science, at a public examination held at Auditorium F239a of the Department of Neuroscience and Biomedical Engineering on 3rd May 2024 at 12 noon.

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Empathy, a socio-cognitive process of perceiving the feelings of others, is one of the fundamental basis of healthy social interaction. Advancements in neuroimaging techniques in the past three decades have facilitated a deeper exploration of the neural mechanisms associated with empathy, complementing traditional approaches and broadening the understanding of this complex phenomenon.

This thesis investigated the intricate neural basis of empathy and its variations across individuals. In Study I, we employed magnetoencephalography (MEG) to explore frequency-decomposed neural activities during pain empathy. We detected four significant patterns corresponding to different components of empathy including an alpha suppression pattern, two beta suppression patterns, and a late alpha-beta enhancement pattern as well as their link to subjective experiences. In Study II, MEG and Functional Magnetic Resonance Imaging (fMRI) were utilized to examine the maturation of empathy, revealing a shift in neural and functional mechanisms of empathy from adolescence to young adulthood. Studies III and IV delved into the association between political ideology and neural responses to emotional suffering and physical pain of others, respectively, highlighting an intriguing, yet complex, relationship between empathy and political ideology. Overall, the findings in the current thesis advance the understanding of neural processes underlying empathy, underscoring the importance of considering diverse factors such as age, political ideology, and subjective experiences. This research can open new vistas for future exploration, encouraging a more comprehensive approach to neuroscientific investigations of empathy.

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Empatia, sosiokognitiivinen prosessi, jossa hahmotetaan toisten tunteita, on yksi terveen sosiaalisen vuorovaikutuksen perustekijöistä. Neurokuvantamis-tekniikoiden kehittyminen viimeisten kolmen vuosikymmenen aikana on mahdollistanut empatiaan liittyvien hermomekanismien syvällisen tutkimuksen, mikä on täydentänyt perinteisiä lähestymistapoja ja laajentanut tämän moni-mutkaisen ilmiön ymmärtämistä.

Tässä väitöskirjassa tutkittiin empatian monimutkaista neuraalista perustaa ja sen vaihtelua yksilöiden välillä. Tutkimuksessa I käytimme magnetoenkefalo-grafiaa (MEG) tutkiaksemme taajuuksittain jaoteltua hermotoimintaa ki-puempatian aikana. Havaitsimme neljä merkittävää mittausta, jotka vastaavat empatian eri komponentteja, mukaan lukien alfa-taajuudella esiintyvä aktiivisuuden vaimentuminen, kaksi beta-taajuudella esiintyvää aktiivisuuden vai-mentumista ja myöhäinen alfa-beta-voimistumisilmiö, sekä näiden yhteys sub-jektiivisiin kokemuksiin.

Tutkimuksessa II käytettiin MEG:tä ja toiminnallista magneettiresonanssikuvausta (fMRI)

empatian kehittymisen tutkimiseen, mikä paljasti empatian neuraalisten ja mekanismien kehittymisen murrosiästä nuoreen aikuisuuteen. Tutkimuksissa III ja IV tutkittiin poliittisen ideologian ja neuraalisten

reaktioiden välistä yhteyttä toisten emotionaalisen kärsimyksen ja fyysisen kivun välillä, mikä toi esiin mielenkiintoisen, mutta monimutkaisen suhteen empatian ja poliittisen ideologian välillä. Kaiken kaikkiaan tämän väitöskirjatutkimuksen tulokset edistävät ymmärrystä empatian taustalla olevista hermostoprosesseista ja korostavat erilaisten tekijöiden, kuten iän, poliittisen ideologian ja subjektiivisten kokemusten, huomioon ottamisen tärkeyttä. Tämä tutkimus voi avata uusia näkymiä tule-valle tutkimukselle ja kannustaa kokonaisvaltaisempaan lähestymistapaan empatian neurotieteellisessä tutkimuksessa.

**Avainsanat** Empatia, Neuraalinen oskillaatio, Alfa-rytmi, Sosiaalinen neurotiede, Neuropoliittikka**ISBN (painettu)** 978-952-64-1777-6**ISBN (pdf)** 978-952-64-1778-3**ISSN (painettu)** 1799-4934**ISSN (pdf)** 1799-4942**Julkaisupaikka** Helsinki**Painopaikka** Helsinki**Vuosi** 2024**Sivumäärä** 132**urn** http://urn.fi/URN:ISBN:978-952-64-1778-3



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Espoo, December 2023  
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# List of Abbreviations and Symbols

ACC	anterior cingulate cortex
AI	anterior Insula
BOLD	blood-oxygen-level-dependent
EC	empathy concern
EEG	electroencephalography
ERPs	event-related potentials
ERD	event-related desynchronization
ERS	event-related synchronization
EPI	echoplanar imaging
fMRI	functional magnetic resonance imaging
GLM	general linear model
ICA	independent component analysis
IFG	inferior frontal gyrus
IRI	interpersonal reactivity index
LCMV	linearly constrained minimum variance
MCC	middle cingulate cortex
MEG	magnetoencephalography
MEP	motor-evoked potentials
mPFC	medial prefrontal cortex
MPRAGE	magnetization prepared rapid gradient echo
MRI	magnetic resonance imaging
NIFTI	neuroimaging informatics technology initiative
NP	no-pain
OFC	orbitofrontal cortex

PaCS	paracentral sulcus
P	pain
PCC	posterior cingulate cortex
PCun	precuneus
PD	personal distress
PT	perspective taking
ROI	region of interest
RWA	right-wing authoritarian
S1	primary somatosensory cortex
SEM	standard error of the mean
SQUIDs	superconducting quantum interference devices
STS	superior temporal sulcus
TE	echo time
TF	time-frequency
TFR	time-frequency representation
TPJ	temporoparietal junction
TR	repetition time
VC	virtual channel
VPQ	vicarious pain questionnaire

# List of Publications

This doctoral dissertation consists of a summary of the following three journal publications as well as one submitted manuscript which are referred to in the text by their Roman numerals.

- I.** Zebarjadi, Niloufar; Kluge, Annika; Adler, Eliyahu; Jääskeläinen, Iiro P.; Sams, Mikko; Levy, Jonathan. 2021. Rhythmic neural patterns during empathy to vicarious pain: Beyond the Affective-Cognitive Empathy dichotomy. Frontiers Media S.A. *Frontiers in Human Neuroscience*, volume 15, pages 380. <https://doi.org/10.3389/fnhum.2021.708107> .
- II.** Zebarjadi, Niloufar; Levy, Jonathan. 2023. Neural shifts in alpha rhythm's dual functioning during empathy maturation. Wiley Periodicals LLC. *Brain and Behavior*, volume 13, issue 9, pages e3110. <https://doi.org/10.1002/brb3.3110> .
- III.** Zebarjadi, Niloufar; Adler, Eliyahu; Kluge, Annika; Sams, Mikko; Levy, Jonathan. 2023. Ideological values are parametrically associated with empathy neural response to vicarious suffering. Oxford University Press. *Social Cognitive and Affective Neuroscience*, volume 18, issue 1, pages 1-10. <https://doi.org/10.1093/scan/nsad029> .
- IV.** Zebarjadi, Niloufar; Kluge, Annika; Adler, Eliyahu; Levy, Jonathan. *New Vistas for the Relationship between Empathy and Political Ideology*. Submitted.

# Author's Contribution

**Study I.** Rhythmic neural patterns during empathy to vicarious pain: Beyond the Affective-Cognitive Empathy dichotomy

AE and LJ designed the experiment and AE collected the data. ZN performed the analysis with the assistance of KA and AE. ZN and LJ interpreted the analysis results. ZN wrote the initial version of the manuscript. ZN and LJ wrote the final version of the manuscript with the approval of all co-authors.

**Study II.** Neural shifts in alpha rhythm's dual functioning during empathy maturation

ZN and LJ planned the experiment. ZN recruited subjects, collected the data, and performed the analysis. ZN and LJ interpreted the analysis results. ZN wrote the initial version of the manuscript. ZN and LJ wrote the final version of the manuscript.

**Study III.** Ideological values are parametrically associated with empathy neural response to vicarious suffering

AE and LJ designed the experiment and AE collected the data. ZN performed the analysis with the assistance of KA and AE. ZN and LJ interpreted the analysis results. ZN wrote the initial version of the manuscript. ZN and LJ wrote the final version of the manuscript with the approval of all co-authors.

**Study IV.** New Vistas for the Relationship between Empathy and Political Ideology

For one experiment, ZN and LJ planned the experiment. ZN recruited subjects, collected the data, and performed the analysis. For the other experiment, AE and LJ designed the experiment and AE collected the data. ZN performed the analysis of this data with the assistance of KA. ZN and LJ interpreted the analysis results. ZN wrote the initial version of the manuscript. ZN and LJ wrote the final version of the manuscript with the approval of all co-authors.



# 1. Introduction

## 1.1 Empathy

The concept of empathy encompasses a broad range of phenomena and psychological capacities, such as perceiving the thoughts and feelings of others, experiencing others' emotional states, caring for others' well-being, and having a willingness to help them (Cuff et al., 2014; Stueber, 2019). Empathic ability plays a crucial role in ensuring the survival of the human species and it is an essential component both at the individual and societal levels (Decety & Jackson, 2004). At the individual level, it is considered a foundation for healthy social interaction by enhancing interpersonal relationships and fostering trust and mutual respect. At the societal level, it is crucial to establish social cohesion by providing effective communication, moderating prejudices, and promoting peaceful conflict resolution (Klimecki, 2019).

Empathy is a complex and multi-faceted socio-cognitive phenomenon. Over the past century, plenty of psychological studies investigated this process by employing behavioral and self-report measures. Through the recent developments in neuroimaging measurement, there has been a growing interest in unraveling the complexity of the brain mechanism associated with the empathy process.

## 1.2 Aims of the study

The primary objective of this thesis is to study neural mechanisms underpinning empathy and investigate how the capacity for empathy varies across individuals, by examining various factors contributing to empathic response. In study I, we utilized neuroimaging techniques, particularly MEG, to evaluate neural activities underlying pain empathy. In addition, we inspected how subjective experiences play a role in shaping empathic responses. In Study II, we examined the maturation of empathy, and particularly we employed MEG and fMRI techniques to investigate the functional meaning of the shift in brain activity pattern associated with empathy during adolescence and young adulthood. In studies III and IV, we explored the intricate interplay between political ideology and the neural basis of various forms of empathy, including empathy for pain and emotional distress.

## 2. Background

### 2.1 History of the concept of empathy

Empathy as a concept gained prominence in the 18th century through the contributions of philosophers such as David Hume and Adam Smith. These philosophers used the term “sympathy” to refer to a phenomenon of understanding and sharing the feelings of others which is nowadays known as empathy (Goldie & Coplan, 2011; Stueber, 2019). In the early 20th century, Theodor Lipps employed the concept of “Einfühlung” which means “feeling into” to elucidate the way individuals experience the mental states of others (Lipps, 1903). Although this German term was first used by Robert Vischer (Vischer, 1873), Lipps began to examine the concept of “Einfühlung” from a psychological and sociological perspective and explained it as a process of inner imitation. The research on “Einfühlung” largely was influenced by Lipps’s works and phenomenologists like Edmund Husserl and Edith Stein criticized and revised Lipps’s account of “Einfühlung” (Husserl, 1931; Stein, 1917). In 1909, cognitive psychologist Edward Titchener introduced the English term “empathy” as a translation of “Einfühlung” (Titchener, 1909). He elaborated on the concept of “empathy” as a process that involves not only understanding other’s minds but also feeling and projecting their mind into one’s own mind (Goldie & Coplan, 2011). In the mid-20th century, standardized scales and measures were developed to quantify empathy, making it a more empirical and measurable concept. Social and developmental psychologists such as Martin Hoffman and Nancy Eisenberg initiated investigations into the role of empathy in prosocial behaviors and identified it as a mediating factor (Eisenberg, 1983; Hoffman, 1977). In parallel, Daniel Batson directed his attention to the moral significance of empathy particularly by presenting the empathy-altruism hypothesis, stating that, in many cases, empathy or “empathic concern” elicits altruistic behavior (Batson, 1997; Batson et al., 2002). During this period investigations on empathy predominantly relied on behavioural and self-report assessments. In the early 1990s, advances in neuroimaging techniques enabled researchers to investigate the brain mechanism underpinning empathy. This indirect and objective measurement approach in conjunction with the traditional approach significantly improved understanding of the empathy phenomenon. The preceding section delves into the historical development of neuroscientific research on empathy.

## 2.2 Brain mechanism underlying empathy

Over the past three decades, the field of neuroscience has yielded notable contributions to studying the processes involved in empathy. Emerging non-invasive neuroimaging techniques such as fMRI and MEG enabled the examination of brain activity associated with empathy with great spatiotemporal resolution. In conjunction with the progress in neuroimaging technologies, the discovery of mirror neurons in the late 1990s by Giacomo Rizzolatti shed light on how the human brain identifies and responds to the mental states of others (Rizzolatti et al., 1996). Mirror neurons comprise a class of neural cells that respond both when a particular action is executed, and when a similar action is observed (Rizzolatti & Craighero, 2004). These neurons are crucial in the process of understanding the vicarious emotional responses by activating similar neural responses in the observer. This phenomenon elucidates the capacity for individuals to unconsciously resonate with other's feelings and has been characterized as the foundation of empathy as noted by Marco Iacoboni (Iacoboni, 2009). In addition, during the 1990s, investigating brain lesions associated with empathy deficits was one of the major areas of interest within the empathy field (S. Shamy-Tsoory & Lamm, 2018). These studies pointed to the involvement of cerebral and frontal lobe lesions as contributing factors to empathy impairments (Grattan et al., 1994) and provided a basis for subsequent investigations on the neural basis of empathy in healthy populations.

In parallel, despite the lack of agreement on the exact definition of empathy among researchers, there is a consensus that empathy is a multifaceted phenomenon encompassing several distinct components (Decety & Jackson, 2004). In numerous studies, two frequently identified components are the "affective" and "cognitive" aspects. The bottom-up affective component involves mirroring another person's emotional state, while the top-down cognitive component pertains to the capacity for mentalization and perspective-taking (Lamm et al., 2007; S. G. Shamy-Tsoory et al., 2009). Later studies suggested "prosocial concern as an additional dimension of empathy, characterized by the motivation to improve vicarious concern (Zaki & Ochsner, 2012). Several studies examined the relation of empathy to prosocial behavior and compassion as a practical implication of studying empathy and emphasized the importance of self-other distinction while studying these phenomena (Hein et al., 2010; Hein, Morishima, et al., 2016; Lamm et al., 2019; Singer & Klimecki, 2014).

In the past few years, there has been an increasing interest in investigating the variations in empathic capacity among individuals as well as examining how differences in brain structure and function are related to these variations (Engen et al., 2018; Frankel, 2017; Patil et al., 2018). For instance, some studies delved into how empathic neural activities vary among age (Levy et al., 2018), and gender (Christov-Moore et al., 2014; Yang et al., 2009). Other studies examined empathy toward ingroups versus outgroups in intergroup relations (Hein et al., 2010; Levy et al., 2016; Perry et al., 2010) or how positive learning experiences modulate empathy-related brain responses toward outgroups (Hein, Engelmann, et al., 2016).

Furthermore, several recent investigations into the neural basis of empathy have made significant progress in designing experiments in naturalistic settings (Goldstein et al., 2018; Jackson et al., 2015; Kozakevich Arbel et al., 2021; Patil et al., 2018). Some of these studies employed virtual reality environments to facilitate more realistic empathic interactions, using interactive avatars (Jackson et al., 2015; Patil et al., 2018).

A brief review of investigations into the neural mechanism underlying empathy with different measurement techniques such as fMRI, MEG, and electroencephalography (EEG) are provided in the next subsections.

### **2.2.1 fMRI measurement**

With the development of the fMRI technique in the 1990s, there has been increasing literature on the brain functional processes associated with empathy using this technique. One of the first studies that employed fMRI to examine the pain empathy process was done by Tania Singer et al. in 2004 (Singer et al., 2004). In the study by Tania Singer et al., they used a que-based paradigm and detected brain regions such as the anterior cingulate cortex (ACC) and anterior insula (AI) both by first-hand pain experience and by watching it in others. Following that, similar results were detected by Jackson and colleagues using picture-based paradigms (Jackson et al., 2005). Subsequent research conducted by Jackson and colleagues suggested that empathy does not involve a complete merging of one's perspective with that of another, but instead, it encompasses a combination of shared as well as distinct cognitive and neural processing (Jackson et al., 2006). Later fMRI studies employed various sorts of paradigms to replicate and improve these findings (Hein & Singer, 2008).

In 2011, a meta-analysis by Lamm and colleagues on 32 fMRI studies on empathy confirmed the role of ACC, middle cingulate cortex (MCC), and AI (extending to the inferior frontal gyrus (IFG)) (Lamm et al., 2011) in sharing and mirroring pain of others, representing the affective aspect of empathy. In addition, investigations into the cognitive aspect of empathy suggested the involvement of the brain area associated with “perspective-taking”, “mentalizing” and “theory of mind”, including the medial prefrontal cortex (mPFC), superior temporal sulcus (STS), and posterior regions such as the temporal parietal junction (TPJ) and precuneus (PCun) and posterior cingulate cortex (PCC) (Bernhardt & Singer, 2012; Lamm et al., 2011). Depending on how empathy is triggered, various components of empathy may be differentially involved (Bruneau et al., 2012; Lamm et al., 2007).

The meta-analysis study by Lamm et al. also offered insights into the debate on somatosensory cortex activation during pain empathy (Lamm et al., 2011). Some earlier studies proposed the engagement of somatosensory and sensorimotor representations in empathetic responses to pain (Keysers et al., 2010), whereas contrasting viewpoints suggested that the shared components between oneself and others primarily involve the affective aspects of pain (Lamm et al., 2011). Lamm et al. indicated that sensory components may play a role when empathy is triggered by robust visual cues depicting situations that

involve the physical manipulation of body parts. Engagement of this brain region was further investigated using electrophysiological measurement techniques.

### 2.2.2 MEG/EEG measurement

EEG and MEG offer valuable insights into the neural underpinnings of empathy, primarily through the exploration of brain oscillations categorized into distinct frequency bands such as theta, alpha, beta, and gamma. Information regarding the characteristics of each brain rhythm is provided in Table 1.

**Table 1.** Characteristics of brain rhythm; frequencies, associated states, and functions.

Rhythm	Frequency range	Associated state	Additional information
Theta	4 to 7 Hz	Deep relaxation, daydreaming	Observed during meditation, light, and REM sleep
Alpha	8 to 13 Hz	Wakeful relaxation	Amplitude decreases during active cognitive tasks, and increases in relaxed states (recent research suggests an amplitude increase during inhibition of task-irrelevant areas in the cortex)
Beta	13 to 30 Hz	Active mental states, cognitive engagement	Observed during tasks requiring concentration
Gamma	More than 30 Hz	High-level cognitive engagement	Observed during tasks involving complex information processing and sensory integration

Investigations utilizing EEG/MEG techniques mainly revealed that particular brain rhythms are associated with distinct facets of empathic processes. Unlike fMRI, these modalities offer an excellent temporal resolution, making them suitable for studying the temporal dynamics of neural mechanisms involved in empathy.

One of the early investigations into the neural substrates underlying empathy for pain indicated the involvement of the primary somatosensory cortex (S1) (Avenanti et al., 2005). This study indicated a suppression in the magnitude of motor-evoked potentials (MEP), that was associated with the observer's self-reported assessment of the sensory aspects of the pain experienced by the protagonist and measures of sensory empathy. In 2008, an EEG investigation into pain empathy while presenting painful versus neutral pictures found that painful compared to neutral stimuli enhances theta event-related synchronization (ERS) and suppresses alpha event-related desynchronization (ERD). ERS and ERD respectively denote a transient increase and decrease in the power of specific frequency bands that occur in response to a stimulus or event. This finding indicated the involvement of theta and alpha brain activity in the pain empathy process (Mu et al., 2008). In the same year, an MEG study by Cheng et al. provided insights into the oscillatory brain activities associated with empathy and

the localized sources (Cheng et al., 2008). This MEG study indicated that perception of vicarious pain suppresses the alpha rhythm activity (~ 10-Hz) in the S1 known as mu rhythm during empathy for pain. Subsequent EEG and MEG studies with various sorts of paradigms replicated this finding and provided additional insights into this observation (Chen et al., 2012; Motoyama et al., 2017; Perry et al., 2010; Whitmarsh et al., 2011).

Although the alpha rhythm has been the predominant focus in empathy research, a limited number of studies have highlighted the engagement of the beta rhythm. Nevertheless, none of these studies elucidated the role of beta oscillations during the empathy process (Levy et al., 2018; Riečanský et al., 2015; Whitmarsh et al., 2011).

### **2.2.3 Multimodal neuroimaging**

As stated in the previous section, recent electrophysiological studies on empathy typically have indicated suppression or enhancement of brain rhythms, particularly the alpha band. One example is a recent MEG study on pain empathy by Levy et al. on subjects with varying age groups. This study detected alpha enhancement in childhood, both low-alpha suppression and high-alpha enhancement in adolescence, and alpha suppression in adulthood. Yet, the functional role of different alpha modulation during empathy across age groups is unclear. To date, there have been no investigations assessing the relationship between brain hemodynamic responses and electrophysiological activities in a specific frequency range during an empathy task.

In the past few years, several studies examined this relationship within the context of other cognitive tasks (Logothetis et al., 2001; Mukamel et al., 2005; Ojemann et al., 2010; Zumer et al., 2010). However, there are contradictory findings on this relation. A number of studies suggested a negative correlation between lower-frequency (e.g. alpha) neural activity and the hemodynamic response in some brain regions, alongside a positive correlation between gamma-frequency neural activity and the hemodynamic response (Mukamel et al., 2005; Scheeringa et al., 2011; Zumer et al., 2010). This is in agreement with the “Gating by inhibition hypothesis” proposed by Jensen et al., which suggests that suppression in alpha activity in a specific brain region reflects active engagement and processing while enhancement in alpha activity indicates inhibition in task-irrelevant regions (Jensen & Mazaheri, 2010). In contrast, a recent review study suggested that brain rhythms exhibit distinct relationships with the blood-oxygen-level-dependent (BOLD) signal across cortical layers (Scheeringa & Fries, 2019). For instance, they proposed separating processes associated with the alpha band in deep and superficial cortical layers. Recently, crossing MEG and fMRI data has emerged as a method for examining this link to provide a comprehensive understanding of brain activities associated with particular cognitive tasks (Kujala et al., 2014; Mathiak et al., 2011; Zumer et al., 2010). MEG allows direct measurement of suppression and enhancement of neural activities in a particular frequency range, while the source localization relies on inverse modeling with certain limitations. Conversely, fMRI’s BOLD estimation pro-

vides exceptional spatial resolution. Therefore, crossing these two neuroimaging techniques allows the localization of the activated and deactivated brain regions associated with the modulation of the frequency decomposed neural activities.

## 2.3 Contributing factors to empathy

### 2.3.1 Age

Empathy, similar to other social and cognitive abilities, emerges in early childhood and develops through interaction with the social environment across the lifespan (Decety & Holvoet, 2021). As discussed in the previous sections, empathy is a multifaceted ability including several components with distinct developmental processes. Some aspects such as sensitivity to emotional signals emerge even during infancy (e.g. crying when they hear other babies cry) (Sagi & Hoffman, 1976), while other aspects require the development of other cognitive and social abilities such as executive function and theory of mind which develop after a few years (Decety & Holvoet, 2021). Adolescence is a critical period for the development of empathy since perspective-taking and moral reasoning undergo significant development during this period (Decety & Holvoet, 2021). These abilities continue to mature during the young adulthood. Over the past two decades, a few neuroimaging studies investigated the brain mechanism associated with empathy throughout the developmental trajectory (Brunsdon et al., 2019; Decety & Michalska, 2010; Levy et al., 2018). In 2010, Decety et al. conducted an fMRI experiment to evaluate age-related differences in brain activation during the empathy process (Decety & Michalska, 2010). They found stronger hemodynamic activity in the amygdala, supplementary motor area, and posterior insula in younger participants compared to older ones and in contrast, stronger activity in the frontal areas was found in the older participants compared to the younger ones. They argued that brain structures related to empathy mature gradually from the amygdala and posterior insula to the dorsal and lateral vmPFC. In 2014, an EEG study on empathic response in children aged 3 to 9 revealed a gradual decline in emotional arousal and affective sharing as well as improvement in cognitive appraisal in children by getting older (Cheng et al., 2014). Later in 2018, a large-sampled developmental MEG study examined neural modulation during empathy from childhood to adulthood and indicated a developmental trend for empathy (Levy et al., 2018). This research detected an enhancement in alpha activity in response to pain compared to neutral stimuli, during childhood. As individuals reached adolescence age, they exhibited a combination of low-alpha suppression and high-alpha enhancement patterns, and eventually, alpha suppression became the predominant pattern, alongside other higher-frequency patterns, in adulthood. They suggested that this trend possibly reflected a gradual shift from self-based sensory processing to other-centered processing of pain empathy. In line with this finding, later developmental investigation into the mirror system confirmed alpha suppression increases in response to pain stimuli, by getting older (Brunsdon et al., 2019).

### **2.3.2 Political ideology**

Individuals with different political ideologies typically vary in their support for social policy issues. Since empathy is the ability to understand the feelings of others and have the desire to help them, it possibly plays a role in fostering support for affirmative action such as promoting equality or providing humanitarian aid. In recent years, a few interdisciplinary studies explored a possible association between political ideology and empathy (Hasson et al., 2018; Morris, 2020; Wagaman & Segal, 2014; Waytz et al., 2016). To date, the findings from these studies are not consistent, with some suggesting a dissimilarity in the level of empathy among individuals with different political ideologies, while other studies have cast doubt on this distinction. For instance, a study by Hasson et al. investigated the interplay between individuals' political beliefs and their empathic-related factors such as motivation to feel empathy, experienced empathy, and willingness to help others (Hasson et al., 2018). Their finding indicated greater motivation for empathy and a higher level of experiencing empathy toward others in liberals compared to conservatives. In agreement with this finding, a study by Wagaman et al. revealed the significant role of interpersonal empathy in people's attitudes toward government intervention (Wagaman & Segal, 2014). Conversely, other studies such as Waytz et al. found no difference between liberals and conservatives in terms of absolute levels of empathy, whereas they suggested that variations in empathic response are due to the differences in the targets of empathy (Waytz et al., 2016). For instance, they indicated that differences in the perspective of each political group on the social world or in their motivational orientations may contribute to a greater inclination for conservatives to empathize with ingroups, such as family, and for liberals to exhibit empathy toward broader social groups. Nevertheless, these investigations predominantly examined the connection through self-reported measures, wherein participants might respond according to the stereotypes or social norms. Hence, employing an objective measure to assess empathy may offer further insights into this relationship.

### **2.3.3 Gender**

In recent years, psychological and neuroscientific investigations into the potential sex/gender disparities in empathic ability have yielded contradictory findings (Christov-Moore & Iacoboni, 2019; Eisenberg & Lennon, 1983; Lamm et al., 2011; Pang et al., 2023; Yang et al., 2009). Typically, studies that relied on self-reported questionnaires to measure empathic ability indicated a higher score in women compared to men (Pang et al., 2023). However, the results of behavioral studies are inconsistent, with some representing a superior rating in women but with a small effect size (Baez et al., 2017) or others indicating greater prosocial intentions in men (Olsson et al., 2021). Similarly, neuroscientific investigations revealed inconsistent findings both among EEG/MEG and fMRI studies (Christov-Moore & Iacoboni, 2019; Han et al., 2008; Lamm et al., 2011; Pang et al., 2023; Yang et al., 2009). For instance, Yang et al. examined sen-

sorimotor activation related to pain empathy with EEG and detected a significantly stronger mu suppression, as a neural marker of empathy, in female compared to male participants (Yang et al., 2009). Another EEG study found similar short-latency empathic responses in males and females and stronger long-latency empathic responses in females than males (Han et al., 2008). In contrast, a recent EEG study reported no difference in the level of empathy across genders (Pang et al., 2023). Among fMRI studies, the meta-analysis by Lamm et al. failed to detect gender disparity in empathic response (Lamm et al., 2011), while other studies found a greater somatomotor response toward vicarious pain in females compared to males (Christov-Moore & Iacoboni, 2019). All in all, these results indicated that variations in empathy based on sex/gender are contradictory and significantly influenced by the assessment method (Baez et al., 2017; Eisenberg & Lennon, 1983). Particularly, the self-reported questionnaires to measure empathic response might be biased (due to the lack of metacognitive insight) (Murphy & Lilienfeld, 2019) or affected by gender-role stereotypes (Baez et al., 2017; Pang et al., 2023).

## **2.4 State and trait empathy**

According to the former investigations into the empathy phenomenon, empathy depends on the interplay between trait and state empathy (Van der Graaff et al., 2016). Trait empathy is the general ability to be empathetic across various situations and over time. It is a relatively stable characteristic and linked to the individual's traits. In contrast, state empathy is a temporary and context-dependent form of empathy in a particular situation, which depends on an individual's current emotional state. These two concepts both play prominent roles in shaping the way individuals empathize with others.

### **2.4.1 Measuring trait empathy**

Trait empathy is typically measured by asking subjects to rate multiple scales in questionnaires. The interpersonal reactivity index (IRI) is one of the questionnaires that is utilized to evaluate trait empathy (Davis, 1983). This measure includes four subscales, each encompassing 7 different items (5-point Likert scale), to examine different aspects of empathy. The subscales are perspective-taking (PT), empathic concern (EC), personal distress (PD), and fantasy.

### **2.4.2 Measuring state empathy**

State empathy is commonly explored by eliciting empathetic responses through behavioral paradigms containing painful stimuli (e.g. images or videos depicting pain). This temporary response is typically measured by questionnaires or neuroimaging techniques. For instance, the vicarious pain questionnaire (VPQ) is a scale to evaluate state empathy and vicarious pain perception (Grice-Jackson et al., 2017). This scale includes 16 videos of people experiencing pain (each lasts approximately 10 seconds). After each video, subjects are asked questions

about their experience of watching the video. In case they report a pain experience in their body while watching the video, they are asked further questions regarding the intensity (10-point Likert scale), location, and type of experienced pain as well as the level of unpleasantness associated with this experience (10-point Likert scale). This measure presents a conceptualization of vicarious pain, specified by variations in phenomenology, and provides the individual differences in the subjective experience of vicarious pain perception. Another example is a test using emotional film clips representing happiness or sadness to evaluate empathy response (Van der Graaff et al., 2016). After each film clip, several questions regarding the quality and intensity of observed and experienced emotions were asked to evaluate affective and cognitive responses to the emotional film clips. In addition to behavioral paradigms, subjective experiences can be also evaluated through phenomenological interviews.

### **2.4.3 Correlation with neural measures**

Previous neuroscientific studies have reported contradictory findings regarding the correlation between trait empathy (mainly IRI measures) and neural results. Several studies suggested the relationship between one or more IRI subscales and neural findings detected by MEG/EEG (Cheng et al., 2008; DiGirolamo et al., 2019; Yang et al., 2009), whereas other studies failed to detect any correlation (Whitmarsh et al., 2011). Even among the studies in the first group, the results are largely inconsistent, some indicating a correlation with EC subscale (DiGirolamo et al., 2019) and others with PT (Cheng et al., 2008) or PD subscale (Yang et al., 2009).

There are limited studies on the evaluation of the correlation between self-reported state empathy and neural results. In the study by Grice-Jackson et al., they detected a link between localized vicarious pain detected by VPQ and brain activity associated with empathy and suggested that the variation of the subjective report is a reflection of differences in brain activity during empathy (Grice-Jackson et al., 2017).

## 3. Materials and methods

### 3.1 Participants

In Study I, III, and a part of Study IV, the research was carried out within the Israeli context. Healthy subjects were recruited via social media for these studies. Before the recruitments, screening procedures were applied to assess MEG compatibility and history of psychiatric and neurological disorders. Participants provided their consent by signing the consent forms before the experiment and individuals were duly compensated for their participation in these studies.

In Study II and the second part of Study IV, the research was conducted in Finland and participants were recruited on the Aalto University campus for this study. Subjects completed an initial online survey to prescreen their compatibility with MEG and fMRI machines and their medical background with regard to psychiatric and neurological conditions. Additionally, their demographic information encompassing gender, age, and political inclination were collected. Participants were provided with a privacy notice and information document and they approved their participation by signing the participation confirmation form. Table 2 provides detailed information on the subjects who participated in each study of this thesis.

**Table 2.** Description of the participants in each study. \*Study II was a registered report study, therefore, the data acquisition ceased after collecting the data from 40 subjects who completed both MEG and fMRI measurements without any technical issues or excessive noises.

Studies	Study I	Study II	Study III	Study IV
Number of subjects (female)	44 (19)	40 (31)	55 (25)	125 (73)
Mean age $\pm$ SD	25.7 $\pm$ 3.94	19.05 $\pm$ 1.66	25.34 $\pm$ 3.87	23.1 $\pm$ 4.44
Political alignment	Not applicable	Not applicable	30 leftists 25 rightists	57 leftists 68 rightists
excluded subjects	1	0*	0	1
Country of Measurement	Israel	Finland	Israel	Finland and Israel
Imaging Modality	MEG	MEG and fMRI	MEG	MEG

In each study, the instructions were provided in the native language of the participants. Studies in the current thesis were approved by either the IDC Herzliya ethics committee or the Aalto University Research Ethics Committee.

### 3.2 Experimental design and stimuli

The same set of well-validated stimuli was utilized in the Study I, II, and IV. These stimuli were previously employed in several empathy experiments (Levy et al., 2016, 2018; Levy, Goldstein, et al., 2019; Pratt et al., 2016; Whitmarsh et al., 2011). It consists of a series of images in the standard uniform size (300 × 225 pixels), half representing the right hands and right feet in painful situations, and the other half was identical images with some minor change that conveys non-painful situations. To maintain the participants' attention during this semi-passive task, a "twirl filler trial" using a small twisted movement in a new set of stimuli was created by Photoshop (Photoshop, Adobe Systems Inc.). Participants underwent training before the measurement to press a response button upon detecting these twirl stimuli. In study II, in addition to the main stimuli, 18 supplementary control images featuring simple landscapes were presented to subjects to assess the contrast between still and action images, thereby, validating that the identified patterns are unique to empathy.

In the experimental design, there are some minor differences between the studies. In Study I and the first dataset of Study IV, the painful and non-painful images were randomly presented at the center of a gray background on a 20-inch monitor for 1 second with an interstimulus interval of 2.5–3.3 s. The experiments were programmed using E-Prime® software (Psychology Software Tools Incorporated). In Study II and the second dataset of Study IV, every three stimuli of the same type were randomly grouped into blocks. Each image was presented at the center of the monitor for 1 second with an interstimulus interval of 3–3.5 seconds, to maximize the detection of the BOLD signal. In total 42 blocks of images with interblock intervals of 15 seconds were displayed. The experiments were programmed and operated by Presentation software (Neurobehavioral Systems, Albany, NY, USA).

In Study III, the paradigm is similar to the paradigm used in a former study to explore the neural mechanism of emotional empathy (Levy, Yirmiya, et al., 2019). Fourteen blocks of emotional suffering and neutral stimuli with an interblock interval of 4–5 seconds were randomly presented to the participants. Each block encompassed a 10-second audio story followed by presenting 8–10 photos related to the story (each lasted for 2 seconds) with an interval of 1–2 seconds. Besides, we matched the stories' length, and the images' physical parameters including complexity, contrast, and luminance as well as the affective valence and arousal of the photos. The programming of the paradigm was done by E-Prime® 2 software (Psychology Software Tools Incorporated).

In all studies, participants were initially introduced to the scanning protocols and instructed to avoid any bodily movements throughout the scanning process.

### 3.3 Magnetoencephalography

MEG is an advanced neuroimaging modality designed for the non-invasive measurement of brain activity by capturing the magnetic field emanating from the electrical activity of the brain. In other words, when neurons in the brain are activated, they produce small electrical currents that generate weak magnetic fields. MEG employs an array of highly sensitive sensors known as Superconducting Quantum Interference Devices (SQUIDS), positioned around the head and close to the scalp to detect the ensuing magnetic fields resulting from neural activities. Remarkably, MEG offers the capability to record cortical activities with a temporal resolution of less than 1 millisecond (Hämäläinen et al., 1993). Besides, by localizing the source of cortical activities, it is possible to detect the engaged brain region with great spatial resolution. The combination of high temporal and spatial resolution positions MEG as a powerful tool for investigating the spatiotemporal dynamics of neural processes.

#### 3.3.1 Data acquisition and preprocessing

Subjects were placed inside the MEG scanner in a magnetically shielded room and instructed to remain still throughout the MEG measurement. Brain activity was captured using a whole-head MEG system, recording data at a sampling rate of approximately 1 kHz. To track head position relative to the sensors, five coils were attached to the participants' scalps. For the studies carried out in Finland, a whole-head 306-channel MEG device (VectorView, Elekta-Neuromag, Helsinki, Finland) at MEG Core of Aalto NeuroImaging infrastructure was employed. During the measurement, a band-pass filter was applied to limit the frequency range to 0.1-330 Hz, and two pairs of electrodes were used to record horizontal and vertical eye movements. In the studies conducted in Israel, a whole-head 248-channel magnetometer array (4-D Neuroimaging, Magnes® 3600 WH) was utilized, and the acquired data band-pass filtered to 1-400 Hz. Besides, reference coils were placed above the head of participants and oriented by the x, y, and z axes to minimize environmental noise.

The preprocessing of the MEG data collected in Israel was performed with MATLAB (MathWorks) and FieldTrip software toolbox (Oostenveld et al., 2011). The preprocessing of the collected data in Finland was done with the MNE-python toolbox (Gramfort et al., 2013) and data were filtered using Max-Filter software (Elekta Neuromag) (Taulu & Simola, 2006) to attenuate measurement artifacts and magnetic interference. In all studies, the independent component analysis (ICA) technique was applied to the collected data to remove eye and heart artifacts, such as eye blinks and movements, and cardiac rhythms. After removing eye and heart components from the data, it was visually inspected to reject any remaining bad trials. Prior MEG studies on empathy typically explored induced oscillatory responses in the time interval of 2 seconds after the stimulus onset and detected empathy effects in this time window (Levy et al., 2018; Whitmarsh et al., 2011). A similar methodological approach was applied in the studies of this thesis and the first 2 seconds after the stimulus

onset was selected as the epoch for assessing empathic brain activity. Additionally, a baseline window of -0.5 to 0 was considered for the analysis.

### 3.3.2 Sensor and source analysis

To determine spectral power, we utilized the multitaper Time-frequency (TF) method by applying a Hanning taper to each trial. We then computed the average power estimates for each experimental condition across the epochs. In the next step, we employed a nonparametric statistical approach (Maris E, 2007) to calculate the statistical contrast between the two conditions and find significant TF windows, while accounting for multiple comparisons. To compare the subjects' results between the conditions, we computed a single averaged power value for each subject by averaging over this significant TF window on the peak sensor.

To localize the sources of brain activity associated with empathy, we employed a beamformer technique. For the studies conducted in Finland, we generated an individualized single-shell brain model for each participant using their magnetic resonance imaging (MRI) data. For the studies conducted in Israel, we utilized the digitized head shape data acquired during MEG measurements (Polhemus FASTRAK® digitizer). In the next step, the grid positions through linear transformation are determined to divide the brain volume into a 1 cm regular grid. At each grid position, beamformer spatial filters were created to pass activity detected within the significant TF window, identified during sensor-level analyses, from the specific area of interest while suppressing activity from other locations. Following the detection of the activity source coordinates, the linearly constrained minimum variance (LCMV) beamformers are applied to compute estimates in the time domain (Van Veen et al., 1997). The spatial filter in the output source structure is multiplied with the original MEG data to reconstruct the single-trial time series as a virtual channel (VC). These source-level time series of activities are examined both for the task and the control conditions. The post-processing of all MEG data was done using MATLAB (MathWorks) and FieldTrip software toolbox (Oostenveld et al., 2011).

### 3.3.3 Statistical analysis

To conduct statistical analysis on the MEG data, we used a cluster-based nonparametric randomization approach (Maris E, 2007). Initially, t-values were computed for each subject, channel, frequency, and time, reflecting the contrast between conditions. Subsequently, the test statistic was defined by pooling the t-values across all participants. TF clusters with statistically significant effects at the random effects level were searched while adjusting for multiple comparisons in both the time and frequency dimensions. The significance of the group-level statistic was assessed using the Monte Carlo technique. This method estimated the significance probabilities by repeatedly randomizing the data between conditions. Specifically, individual t-values were randomly multiplied by 1 or -1, corresponding to permutations of the original conditions within each

subject, and summed over all participants. This randomization process was iterated 1000 times, leading to the construction of a test statistic histogram for the group-level statistic called permutation distribution. Finally, the permutation p-value was determined by calculating the proportion of random partitions in which the observed test statistic exceeds the value drawn from the permutation distribution.

### **3.4 Structural and functional magnetic resonance imaging**

Magnetic resonance imaging (MRI) is a technique that employs a strong magnetic field to form a detailed three-dimensional image of the internal structures of the body. The human body is primarily composed of water molecules containing hydrogen atoms, and the hydrogen protons in these atoms have a property known as spin, causing them to behave like small magnets. When the subject is placed in the MRI machine, a magnetic field is applied, which aligns the magnetic moments of the hydrogen protons in the body with the magnetic field's direction. By applying a brief radiofrequency pulse to the body, the alignment of the protons is disrupted, leading to energy absorption. Upon cessation of the radiofrequency pulse, the protons release the absorbed energy and return to their original alignment. This process results in the emission of radiofrequency signals, that are detected by the MRI machine. Different body structures such as organs, muscles, and soft tissues exhibit unique relaxation times, resulting in signal intensity variations. These signals are used to generate high-resolution MRI images (Huettel et al., 2004).

Functional MRI extends the utility of MRI to evaluate brain activity changes over time by measuring the changes in blood flow and blood oxygenation levels. Neurons in a particular brain region become active while performing a task or processing information and require more oxygen. This increased neural activity leads to an increase in the blood flow in the active regions to deliver oxygen. Due to the different magnetic properties of the oxygenated and deoxygenated hemoglobin, the changes in the concentration of oxygenated hemoglobin in the brain region affect the local magnetic field. The fMRI technique relies on the contrast in this hemodynamic signal, called blood oxygen level-dependent (BOLD), that captures the magnetic properties of hemoglobin (Huettel et al., 2004). fMRI acquires a series of images over time and creates a dynamic map of brain activity to identify areas of the brain with increased or decreased activity during a particular task or process.

fMRI studies typically acquire both structural and functional MRI scans and align the functional images with the corresponding structural MRI image to precisely examine brain activation across the brain and regions of interest.

#### **3.4.1 Data acquisition and preprocessing**

In study II, structural and functional MRI data were collected using a 3 Tesla MRI scanner (MAGNETOM Skyra, Siemens Healthcare, Erlangen, Germany)

and a 30-channel receiving head coil array at Aalto University's Advanced Magnetic Imaging (AMI) Centre. Participants lay down on a table that moved into the magnet's core, viewing stimuli on a screen positioned 33–35 cm away through an overhead mirror. Structural MRI data was measured using a high-resolution T1-weighted magnetization prepared rapid gradient echo (MPRAGE) pulse sequence in sagittal orientation with repetition time (TR) = 2530 ms, echo time (TE) = 3.3 ms and 176 slices with a thickness of 1.5 mm. functional MRI data was acquired using a T2\*-weighted echoplanar imaging (EPI) sequence in transverse orientation with TR = 1260 ms, TE = 32 ms, flip angle = 62° and 40 slices with the thickness of 3 mm. Stimuli were presented using Presentation software (Neurobehavioral Systems, Albany, NY, USA), and fMRI data was analyzed by MATLAB 2020 and SPM12 toolbox ([www.fil.ion.ucl.ac.uk/spm](http://www.fil.ion.ucl.ac.uk/spm)).

To process the data with the SPM toolbox, the data was converted into the neuroimaging informatics technology initiative (NIFTI) format. A standard fMRI data preprocessing protocol was applied to the functional brain images. Initially, slice-time correction and motion correction were applied to the data. In parallel, structural images were corrected and skull-stripped. In the following step, the functional and structural MRI images were coregistered to accurately localize the neural activity. In the final step, data were normalized to a standard space, and spatial smoothing with an 8-mm full-width at half-maximum Gaussian kernel was applied to the data.

### 3.4.2 Data analysis

The general linear model (GLM) is a mathematical approach that models the BOLD activity as a weighted sum of the experimental conditions (Huettel et al., 2004). By applying this approach, brain responses can be modeled as a linear combination of multiple regressors, which together form a design matrix. Through GLM analysis, regression coefficients are estimated in a way that minimizes the differences between the design matrix and the measured data. By fitting the design matrix to the fMRI data, activated brain regions associated with each experimental condition can be detected.

To analyze the fMRI data in Study II, the GLM was applied to the preprocessed data. Initially, the contrasts between the pain and no-pain conditions were calculated for each subject. Next, a statistical t-test between the conditions over the mean parameter estimates from each subject was conducted to examine the contrast at the group level and detect the activated/deactivated brain regions. Subsequently, the peak coordinates of the most significant brain regions were extracted for the region of interest (ROI) analysis. To further investigate these coordinates, we utilized the MarsBaR toolbox (Brett et al., 2002) to perform spherical ROI analyses. In this ROI approach, we generated 5 mm diameter spheres centered on each extracted coordinate. These spheres were employed as masks to assess the average activity across the voxels within the selected regions for each experimental condition. Significance testing via a statistical t-test on the average activity levels between the two conditions was conducted to evaluate the degree of difference within each selected region.

### 3.5 Self-reported assessments

Multiple self-reported measures were employed in the research presented in this thesis to assess both trait and state empathy, along with other variables such as political attitudes.

The evaluation of trait empathy involved the utilization of the EC and PT subscales from the IRI questionnaire (Davis, 1983). The items are provided in Table 3 and participants rated the extent they agree or disagree with the statements. The negative items were scored in reverse fashion.

**Table 3.** Items from the IRI scale were used in the studies of this thesis (Davis, 1983).

Number	Sub-scale	Polarity	Item
1	EC	Positive	I often have tender, concerned feelings for people less fortunate than me.
2	PT	Negative	I sometimes find it difficult to see things from others' point of view.
3	EC	Negative	Sometimes I don't feel very sorry for other people when they are having problems.
4	PT	Positive	I try to look at everyone's side during a disagreement before I make a decision.
5	EC	Positive	When I see someone being taken advantage of, I feel kind of protective towards them.
6	PT	Positive	I sometimes try to understand my friends better by imagining how things look from their perspective.
7	EC	Negative	Other people's misfortunes do not usually disturb me a great deal.
8	PT	Negative	If I'm sure I'm right about something, I don't waste much time listening to other people's arguments.
9	EC	Negative	When I see someone being treated unfairly, I sometimes don't feel very much pity for them.
10	PT	Positive	I believe that there are two sides to every question and try to look at them both.
11	PT	Positive	When I'm upset at someone, I usually try to "put myself in his shoes" for a while.
12	PT	Positive	Before criticizing somebody, I try to imagine how I would feel if I were in their place.

To examine state empathy, we used 7 videos of the VPQ scale (Grice-Jackson et al., 2017). After each video, participants were asked the following questions:

1. Did you experience any bodily sensation of pain whilst observing the person in pain?
2. Please rate how painful this experience was for you. (Likert scale, 1= Very Mild Pain, 10= Highly intense pain)
3. How unpleasant did you find the experience of watching this video? (Likert scale 1= not unpleasant, 10= Highly unpleasant) (Grice-Jackson et al., 2017)

To evaluate the political attitude, subjects were asked to rate their general political ideology on a seven-point scale ranging from 1 (extreme rightist) to 7 (extreme leftist).

Subsequently, they were asked to rate the adopted 7 items from the right-wing authoritarian (RWA) scale (Altemeyer, 1983) to measure the extent to which the subject supports and adheres to traditional values endorsed by authorities. According to previous research, higher scores on this scale are associated with a higher tendency toward right-wing political ideology (Manganelli Rattazzi et al., 2007). The items that were used are provided in Table 4. Similar to IRI, the negative items were scored in reverse fashion.

**Table 4.** Items from the RWA scale were used in the studies of this thesis (Altemeyer, 1983).

Number	Polarity	Item
1	Positive	The only way our country can get through the crisis ahead is to get back to our traditional values, put some tough leaders in power, and silence the troublemakers spreading bad ideas.
2	Negative	Our country needs free thinkers who have the courage to defy traditional ways, even if this upsets many people.
3	Positive	Our country will be destroyed someday if we do not smash the perversions eating away at our moral fiber and traditional beliefs.
4	Negative	Everyone should have their own lifestyle, religious beliefs, and sexual preferences, even if it makes them different from everyone else.
5	Positive	This country would work a lot better if certain groups of troublemakers would just shut up and accept their group's traditional place in society.
6	Negative	There is no "one right way" to live life; everybody has to create their own way.
7	Positive	The "old-fashioned ways" and the "old-fashioned values" still show the best way to live.

## 4. Summaries of studies

### 4.1 Study I: Rhythmic neural patterns during empathy to vicarious pain: Beyond the Affective-Cognitive Empathy dichotomy

#### 4.1.1 Aim of the study

The primary objective of this study is to investigate the nature of pain empathy to evaluate whether it is a dichotomous phenomenon or can extend beyond the dualistic affective-cognitive perspective and be considered a graded phenomenon with multiple dimensions. In this MEG study, a set of painful versus neutral stimuli was presented to the participants, and the brain empathic responses in relatively broad time and frequency ranges, as well as the cortical sources of the activities, were examined. Moreover, the subjective experience of sensitivity to other's pain and the level of trait empathy were assessed in participants to explore potential connections between neural processes and individuals' subjective experiences and self-reported findings. This research introduces a novel approach and provides empirical support for unraveling the intricate dynamics of empathy.

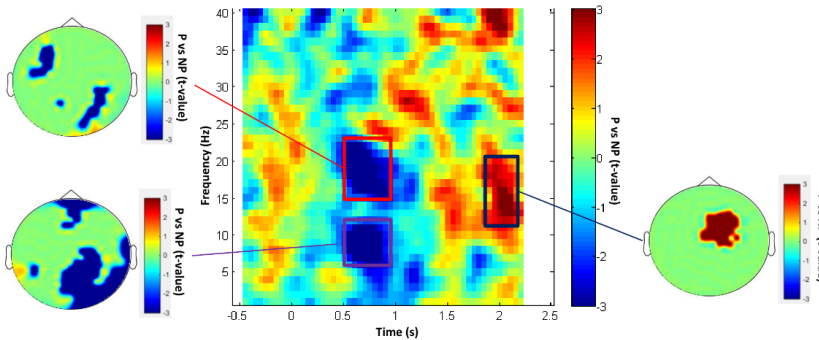
#### 4.1.2 Experimental setup

This study consists of MEG measurement and behavioral evaluation phases, conducted on the forty-four participants (19 females, mean age  $\pm$  SD = 25.7  $\pm$  3.94 years). During the MEG measurement, subjects' neural oscillations, while observing painful versus neutral stimuli were assessed. Stimuli consisted of 96 well-validated color images, half depicting limbs in painful conditions and half in neutral conditions. The purpose of the pain (P) condition was to evoke feelings of empathy, while the no-pain (NP) condition served as a control to account for other visual stimulus-related variables. To maintain participants' attention, a "twirl filler trial" was added.

In the behavioral phase, we first measured participants' empathic traits by asking them to rate the EC and PT subscales of the IRI questionnaire (Davis, 1983). Secondly, we assessed participants' subjective sensitivity to vicarious pain using VPQ assessment (Grice-Jackson et al., 2017). The average scores for the IRI and VPQ measures were computed.

### 4.1.3 Results

The sensor analysis on the whole sensor array in the broad TF window of 0–2.5 s and 1–150 Hz revealed three significant patterns ( $P_{\text{cluster-corr}} < 0.05$ ) in response to observing contrasting stimuli. As illustrated in the statistical time-frequency representation (TFR) and topographies of averaged  $t$ -values on each significant pattern in Figure 1, the early alpha suppression pattern was detected over the central-posterior area, the early beta suppression pattern was found in several non-localized sensors, and the late alpha/low-beta enhancement pattern was indicated in the anterior-central area.

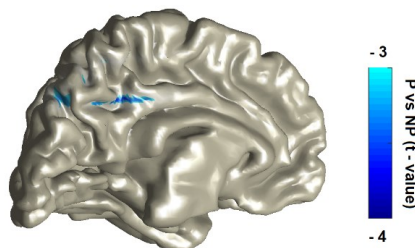


**Figure 1.** TFR contrast between the conditions and topographical maps for each statistically significant TF pattern, represented by rectangles ( $P_{\text{cluster-corr}} < 0.05$ ). (From Publication I (Zebarjadi et al., 2021))

Source localization of each significant pattern revealed neural modulation in the following brain region:

1. Psulcus (PaCS) for the alpha suppression pattern ( $P_{\text{cluster-corr}} = 0.09$ , permutation test)
2. MCC and PCun for the beta suppression pattern ( $P_{\text{cluster-corr}} < 0.05$ , permutation test)
3. Orbitofrontal cortex (OFC) for the alpha-beta enhancement pattern ( $P_{\text{cluster-corr}} = 0.09$ , permutation test).

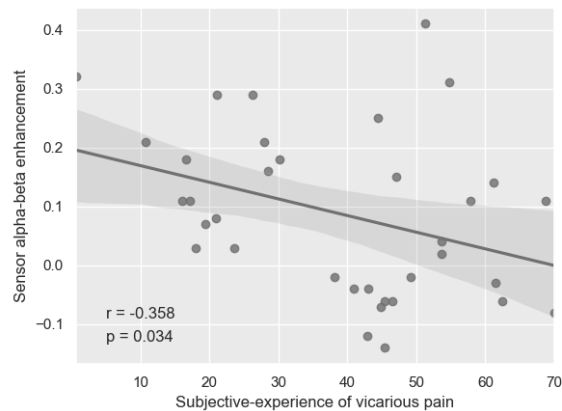
The two sources of beta suppression are visualized in Figure 2.



**Figure 2.** Source localization of the beta suppression effect with two main peaks ( $P_{\text{cluster-corr}} < 0.05$ , permutation test). (From Publication I (Zebarjadi et al., 2021))

According to the former empathy studies, the alpha suppression pattern possibly reflects sensory processing in the central brain region (Whitmarsh et al., 2011), the two beta suppression patterns in the MCC and PCun plausibly indicate the affective and cognitive components of empathy (Fauchon et al., 2019; Lamm et al., 2011), respectively, and the enhancement pattern plausibly reflects cognitive-control inhibitory response (Hooker & Knight, 2006; Schubring & Schupp, 2021).

By correlating the behavioral results with the sensor-source neural findings, a significant negative correlation between the participants' subjective sensitivity to vicarious pain and their late alpha-beta power enhancement during the experiment was found ( $r = -0.358$ ,  $p = 0.034$ ) and indicated in Figure 3. This correlation suggests the potential discovery of a new inhibitory neural mechanism specifying the subjective sensitivity to others' pain.



**Figure 3.** Parametric representation of alpha-beta power enhancement emanated from the orbitofrontal cortex as a function of the subjective experience of vicarious pain in participants ( $r = -0.358$ ,  $p = 0.034$ ). (From Publication I (Zebarjadi et al., 2021))

#### 4.1.4 Conclusion

In this study, we found several rhythmic patterns for empathy, sensory alpha suppression pattern, and frontal inhibitory alpha-beta power enhancement pattern as well as beta power suppression patterns from affective and cognitive networks, although the alpha cortical localization effect yielded a statistical trend. These findings suggest a complex, multifaceted rather than a dichotomous representation of pain empathy. This complexity is supported by the absence of correlations between the neural response and self-reported trait empathy and the presence of a negative correlation between the OFC alpha-beta power enhancement and subjective experiences. The detected correlation suggests an inhibitory control mechanism in the perception of painful stimuli, which serves to regulate emotions and social behavior.

## 4.2 Study II: Neural shifts in alpha rhythm's dual functioning during empathy maturation

### 4.2.1 Aim of the study

This registered report study aimed to elucidate the functional meaning of the observed shift in brain activity patterns during empathy tasks, as previously identified in a neurodevelopmental study (Levy et al., 2018). Our investigation involves the measurement of neural activities in consecutive MEG and fMRI sessions among adolescents and young adults. The first objective was to examine the potential correspondence between low-alpha suppression and functional activation during the experience of pain empathy. The second objective was to explore the relationship between the recently observed high-alpha enhancement in developmental empathy studies and the corresponding BOLD activity during empathy tasks in adolescents and young adults. The involved brain areas detected by each modality were employed to examine the ROI in the other imaging modality. Furthermore, we employ behavioral assessments to evaluate empathic traits and sensitivity, examining the potential contribution of individual variations. This study enhances the understanding of the neural mechanisms underlying empathy with potential implications for future investigations into the developmental aspect of empathy.

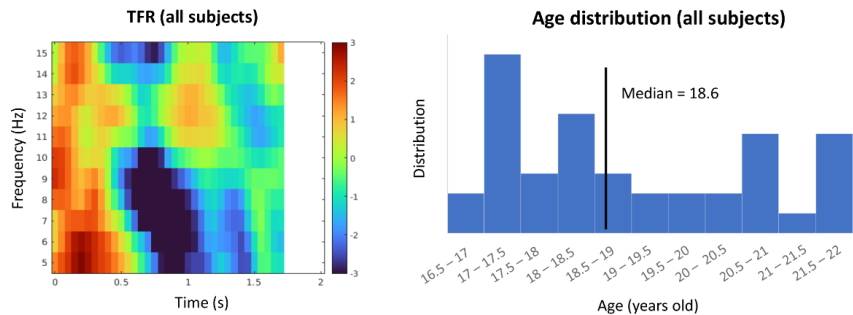
### 4.2.2 Experimental setup

In this study, 40 participants (31 females, mean age  $\pm$  SD = 19.05  $\pm$  1.66 years), initially underwent MEG recording, followed by fMRI scanning. The same task design was implemented in both MEG and fMRI experiments to enhance the reliability of data alignment between the two modalities. A total of 126 images were presented to the participants with 54 depicting physical pain in the body (i.e. P condition), 54 identical images except with minor changes that resulted in conveying NP condition, and 18 landscape images to confirm that alpha activity patterns are unique to empathy. To maximize the detection of the BOLD signal, we employed a block design approach. The stimuli were organized into 42 blocks, each consisting of three stimuli of the same type. Additionally, we incorporated an attentional random twirl task to engage participants in this semi-passive task, a common practice in similar experiments.

### 4.2.3 Results

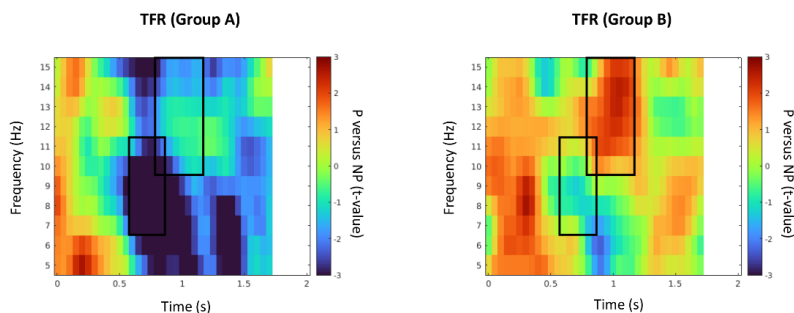
The initial assumption of this research was that the shift in the pattern of brain activity during empathy happens around the age of approximately 20 years. Nevertheless, through the implementation of whole-brain TFR analysis within the alpha frequency range, as illustrated in Figure 4, no significant high-alpha power enhancement was detected (negative  $p_{\text{cluster-corr}} = .018$ ,  $T = -5.489$  and positive  $p_{\text{cluster-corr}} = .394$ ,  $T = 2.1$ , permutation test). This implies that the observed pattern is similar to the brain activity pattern seen in previous studies involving adult subjects and the age group is not young enough to examine the second objective of this study. Consequently, we divided our subjects

into two groups based on the median age. The age distribution histogram of all subjects is provided in Figure 4. This approach allowed for assessing whether any enhancement pattern could be detected for the younger group and determining if there were statistically significant differences in the TF results between these two groups.



**Figure 4.** The left figure represents the TFR contrast between the conditions for the whole sample ( $n=40$ ) and the right figure illustrates the age distribution histogram. (From Publication II (Zebarjadi & Levy, 2023))

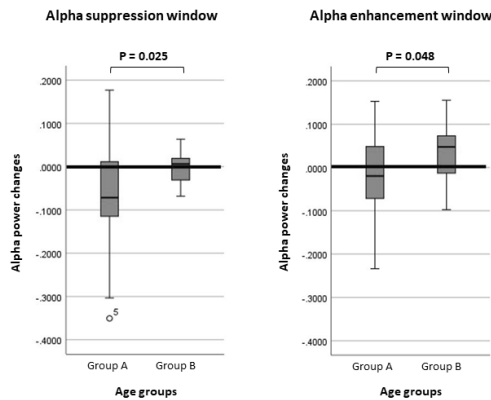
The older group (group A) comprised individuals aged 18.6–22 years ( $n = 20$ , 15 females;  $M \pm SD$ ,  $20.5 \pm 1.03$ ), while the younger group (group B) consisted of individuals aged 16–18.6 years ( $n = 20$ , 16 females;  $M \pm SD$ ,  $17.6 \pm 0.58$ ). As shown in Figure 5, for group A, the statistical contrast between the P and NP conditions indicated a highly significant result (negative pcluster-cor = .006,  $T = -6.64$ , permutation test), and a significant suppression was observed in the TF range of ( $f = 7\text{--}11$  Hz,  $t = 0.6\text{--}0.85$  s). In contrast, for group B, the enhancement pattern was shown to be statistically significant (positive pcluster-cor = .026,  $T = 2.503$ , permutation test) in the TF window of ( $f = 10\text{--}15$  Hz,  $t = 0.8\text{--}1.15$  s).



**Figure 5.** TFR contrasts between the conditions for each group of participants. The black rectangles represent detected low-alpha suppression and high-alpha enhancement windows. (From Publication II (Zebarjadi & Levy, 2023))

The comparison between age groups regarding the average power over the detected TF windows is indicated in Figure 6. Over the suppression window, the results revealed significantly greater suppression in group A compared to group B ( $p = .025$ ,  $T = -2.41$ , independent T-test). Similarly, over the enhancement

window, findings indicated notably lower enhancement in group A compared to group B ( $p = .04$ ,  $T = -2.05$ , independent T-test).



**Figure 6.** Barplots for the averaged power over each window, in groups A and B. (From Publication II (Zebarjadi & Levy, 2023))

By localizing the sources of activities in both age groups over the detected TF window, we found that in group A, MEG sources emanated from the left motor cortex (extending into left S1), left posterior cingulate cortex (PCC), and approximately left supramarginal gyrus (negative pcluster-cor = .04,  $T = -3.56$  permutation test). We used the detected peak coordinates in MEG to examine the fMRI ROI analysis. Contrary to the initial expectations, the results of the fMRI ROI analysis did not confirm the association between low-alpha suppression and BOLD activation for these MEG sources. In the next step, we evaluated GLM analysis in fMRI data. In contrast to MEG to fMRI analysis, fMRI to MEG analysis indicated that the low-alpha suppression corresponds to the BOLD activation and revealed alpha power suppression in two coordinates extracted from the fMRI data analysis, at the right S1 (pcluster-cor = .034,  $T = -2.93$  permutation test) and left motor cortex (pcluster-cor = .032,  $T = -3.2$  permutation test). In group B, The MEG source localization revealed two high-alpha power enhancement sources (without multiple comparison corrections) at the right ACC and left PCC. Intriguingly, by conducting fMRI ROI analysis, we observed a significant decrease in BOLD signal, indicating deactivation in these brain regions (source 1:  $p = .004$ ,  $T = 3.25$ ; source 2:  $p = .040$ ,  $T = 2.21$ ; paired sample T-test). In agreement with this analysis, the fMRI to MEG analysis indicated significantly less alpha power suppression for the pain compared to the neutral condition in the areas detected by fMRI investigation, including right PCC (pcluster-cor = .029,  $T = 2.57$  permutation test) and left PCC (pcluster-cor = .002,  $T = 3.23$  permutation test) and right S1 (pcluster-cor = .035,  $T = 2.37$  permutation test).

#### **4.2.4 Conclusion**

These findings suggest that the brain mechanism associated with empathy experiences a transition by age, from high-alpha power enhancement and functional inhibition to low-alpha power suppression and functional activation within specific brain regions. This observed shift in brain activity from adolescence to adulthood potentially signifies empathic maturation at the age of approximately 18 years. These novel findings indicate an inhibitory control mechanism in adolescents during the empathy process which diminishes in adulthood and can provide a foundation for future investigations on the electrophysiological and functional brain activities during empathy maturation.

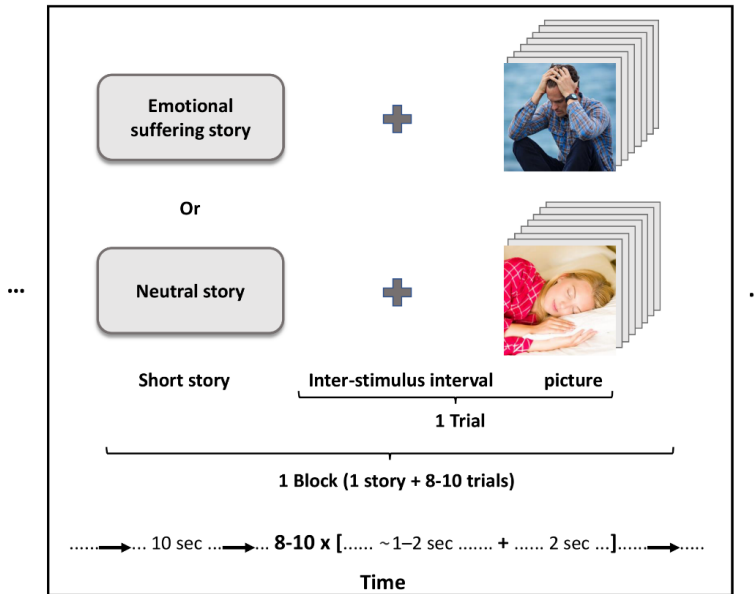
### **4.3 Study III: Ideological values are parametrically associated with empathy neural response to vicarious suffering**

#### **4.3.1 Aim of the study**

The main objective of this study is to investigate the interplay of the neural response underlying empathy toward vicarious emotional distress and political ideology, using neuroimaging techniques, namely MEG. In addition, we examine whether the source of the detected neural response is localized in a brain region associated with mentalizing and cognitive empathy. Several prior self-reported studies indicated differences in psychological abilities, such as empathy, between opposing political groups (Hasson et al., 2018; Morris, 2020). However, the self-reported studies might carry subjective bias and participants might not report their true beliefs due to conformity to social norms (Brandt et al., 2014; Jost et al., 2014). The current study addresses this asymmetry by employing neuroimaging as an objective and unbiased tool to evaluate empathic abilities.

#### **4.3.2 Experimental setup**

In this study, empathy toward vicarious emotional suffering was measured by the MEG technique. During the brain measurement, 55 participants (25 females, mean age  $\pm$  SD = 25.34  $\pm$  3.87 years) were exposed to two distinct experimental conditions and instructed to adopt the perspective of the depicted target. The paradigm included seven emotional suffering and seven control blocks, randomly presented to the participants. As illustrated in Figure 7, Each block consisted of a brief narrative followed by a series of related images, and the narratives were designed to contextualize the subsequent images. A total of 128 images of emotional suffering and neutral conditions in a uniform size were displayed to the participants. The inter-block and inter-stimulus intervals were approximately 4-5 and 1-2 seconds, respectively.

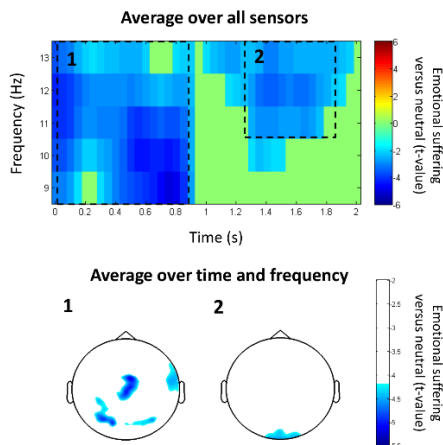


**Figure 7.** The experimental design of one block of paradigm used during MEG measurement. (From Publication III (Zebarjadi et al., 2023))

Furthermore, participants rated several scales related to political ideology, such as the political ideology scale and the RWA scale.

### 4.3.3 Results

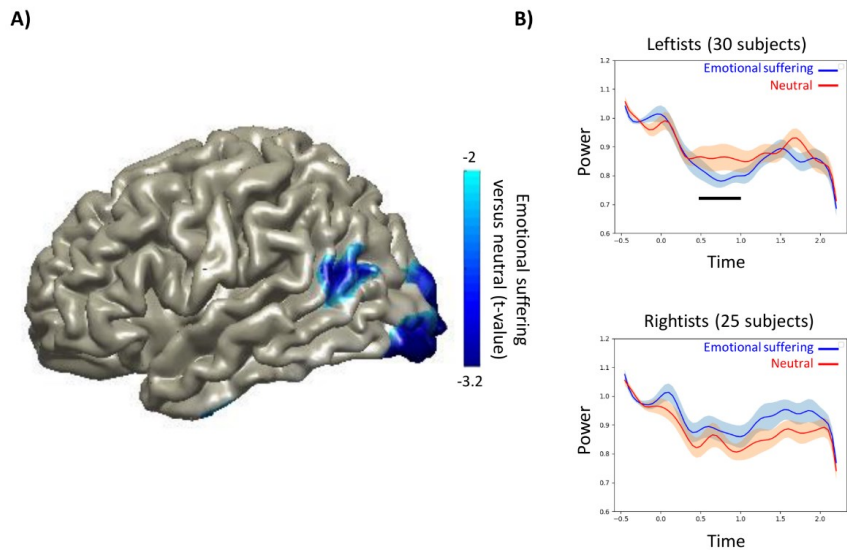
Sensor analysis in the alpha-band frequency range across all MEG sensors revealed two distinct alpha suppression patterns, one in the time window of 0–850 ms ( $P_{\text{cluster-cor}} = 9.9900e-004$ , permutation test) and the other in the time window of 1250–1850 ms ( $P_{\text{cluster-cor}} = 0.0020$ , permutation test). The TFR and scalp topographies are illustrated in Figure 8.



**Figure 8.** TFR contrast between the conditions in the alpha range for the whole sample and the scalp topography for each TF window. (From Publication III (Zebarjadi et al., 2023))

The source analysis was conducted on the first pattern based on the greater robustness of this pattern, topographies of both patterns and former MEG study employing the same empathy paradigm (Levy, Yirmiya, et al., 2019).

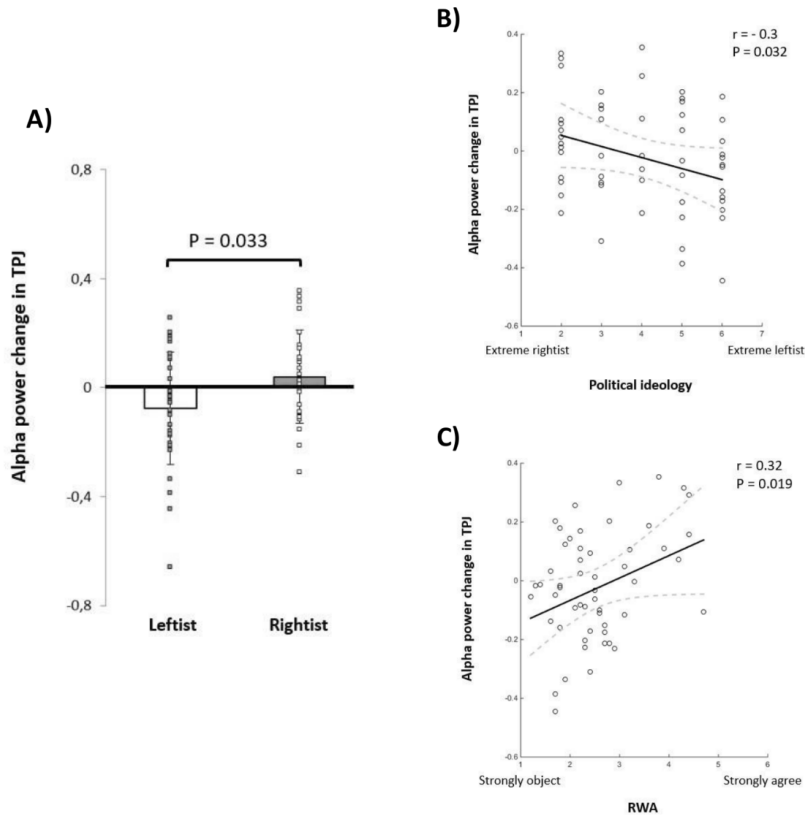
As illustrated in Figure 9A, the suppression was observed to originate from two cortical sources. The peak of the primary source was localized in the left TPJ and extended to the left STS ( $P_{\text{cluster-cor}} = 0.0190$ , permutation test). According to the literature, the TPJ is one of the main brain areas involved in processes related to cognitive empathy, mentalizing, and theory of mind (Marsh, 2018; Zaki & Ochsner, 2012). Therefore, in the context of this investigation, TPJ suppression may serve as a neural marker of empathy toward vicarious distress. In addition, another peak was detected in the occipital region ( $P_{\text{cluster-cor}} = 9.9900e-04$ ), which presumably corresponds to the perceptual and attentional processes during the task (da Silva, 2013). To investigate the temporal evolution of the alpha activity in TPJ during the empathy task among individuals with differing political affiliations, we conducted VC analysis on the peak coordinate, of each political group. Figure 9B indicates alpha temporal changes for each group, with significant alpha suppression for the leftist group ( $P_{\text{cluster-cor}} = 0.004$ ) and conversely, no significant alpha suppression for the rightist group ( $P_{\text{cluster-cor}} = 0.0160$ ). In addition, we conducted VC analysis on the two other coordinates in the left TPJ, reported in previous studies with similar stimuli (Hynes et al., 2006; Saxe & Kanwisher, 2003), and found consistent results.



**Figure 9.** A) Source localization of alpha activities for the whole sample. B) Temporal changes of alpha power (baseline corrected) in response to vicarious emotional suffering (blue line) and neutral (red line) stimuli for each political group. The shades in Figure B represent the standard error of the mean (SEM), and the thick black line indicates the significant effect ( $P_{\text{cluster-cor}} < 0.001$ ). (From Publication III (Zebarjadi et al., 2023))

Statistical t-tests between the averaged alpha power changes in TPJ, over the significant time window, for subjects of the two political groups indicated a significant difference between groups ( $P = 0.033$ , independent T-test), as shown in Figure 10A.

In addition, we conducted the correlation between the alpha power changes in TPJ and two self-reported political scales to evaluate whether the difference is dichotomous or parametric. As illustrated in Figure 10B, the correlation between the neural effect and the political ideology self-reported values suggested that the greater inclination toward leftist' ideology is associated with greater alpha suppression in the TPJ area, and therefore, a greater level of emotional empathy ( $r = -0.3$ ,  $P = 0.032$ ). The correlation between the neural effect and the RWA scale, as represented in Figure 10C, indicated that the greater inclination toward right-wing values is correlated with less alpha suppression in TPJ, representing less emotional empathic response ( $r = 0.32$ ,  $P = 0.019$ ).



**Figure 10.** A) Statistical contrast between averaged alpha power suppression of the two political groups ( $P = 0.033$ ), B) Parametric representation of the neural effect of pain empathy as a function of political ideology ( $r = -0.3$ ,  $P = 0.032$ ), and C) Parametric representation of the neural effect of pain empathy as a function of self-reported RWA ( $r = 0.32$ ,  $P = 0.019$ ). (From Publication III (Zebarjadi et al., 2023))

#### 4.3.4 Conclusion

In the present investigation, neural responses were assessed emotional empathy task, revealing a statistically significant brain activation centered in the TPJ. This observation is consistent with numerous prior findings (Bernhardt & Singer, 2012; Perner et al., 2006; Samson et al., 2004). We observed a significantly stronger TPJ involvement, and thereby neural empathic response in the

leftist group as opposed to the rightist group. This effect was influenced by the degree of political disposition as well as the inclination toward right-wing values. This finding supports the former self-reported observations on this topic and might be linked to the moral foundation and fundamental ideological differences between these two political groups. Nevertheless, an alternative social context or experimental design might result in different neural responses.

#### **4.4 Study IV: New Vistas for the Relationship between Empathy and Political Ideology**

##### **4.4.1 Aim of the study**

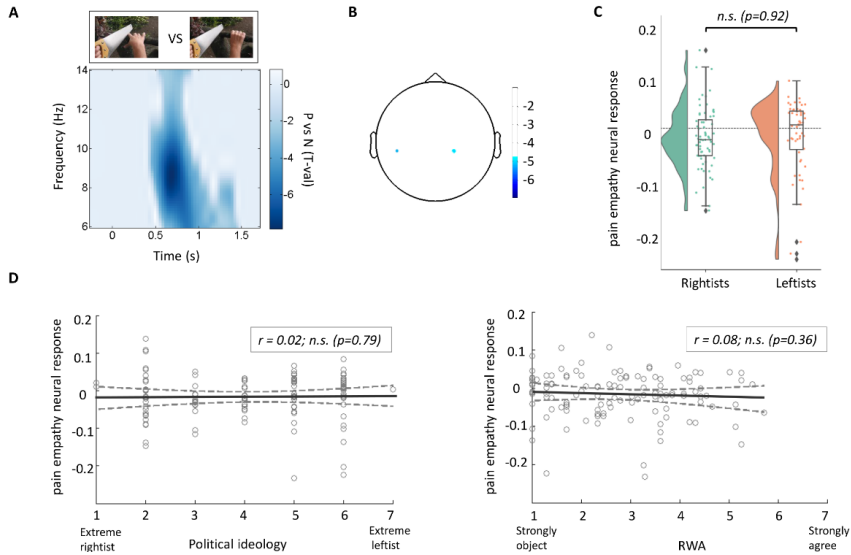
This study seeks to extend current research on the association between empathy and political ideology and provide a more comprehensive insight into this association. A large group of subjects from two different countries participated in this study and their brain activities while observing vicarious physical pain were recorded by MEG. The experimental paradigm employed in this study is different from the one used in Study III to examine whether the previous finding can be generalized to any form of empathy, e.g. physical pain empathy, or it is limited to empathy toward vicarious emotional suffering. In addition to brain recording, we employed several behavioral measures to evaluate empathic response.

##### **4.4.2 Experimental setup**

This research was conducted on in total of 125 subjects (73 females; mean age  $\pm$  SD,  $23.1 \pm 4.44$ ), 77 in Israel and 48 in Finland. One participant was excluded from the study due to huge noises caused by the dental wire. The experimental designs and stimuli were similar to Study I and II with some minor differences. After the neuroimaging session, participants filled out several questionnaires to evaluate their empathic level and ideology. Among all subjects, 68 participants identified as rightists and 57 as leftists.

##### **4.4.3 Results**

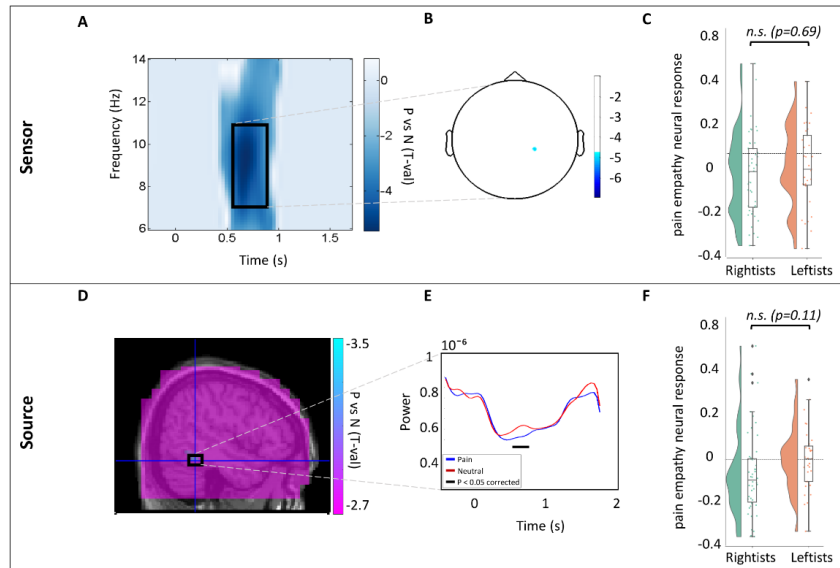
Sensor analysis conducted on all participants revealed a significant alpha suppression pattern within the time frame of 500 to 900 ms (negative  $P_{\text{cluster-cor}} < 0.001$ ,  $T = -7.74$ , permutation test), shown in Figure 11A. The topographic representation of MEG sensor data for each dataset is depicted in Figure 11B. To examine the empathy difference between the two political groups, the averaged power contrast values in the significant TF window for individuals belonging to each group were calculated ( $p = 0.92$ , independent T-Test) and illustrated in Figure 11C. Furthermore, by correlating the sensor neural finding with the self-reported political ideology and RWA scales, we observed a non-significant correlation between the empathy neural effect and self-reported political metrics. These findings are contrary to the findings reported in the study III.



**Figure 11.** Pain Empathy – the neural response. A) TFR contrast between the two conditions. B) Topographic contrasts in each dataset. C) Raincloud histograms of pain empathy per each political group D) Parametric representation of pain empathy as a function of political ideology self-reports (left panel) and RWA ratings (right panel).

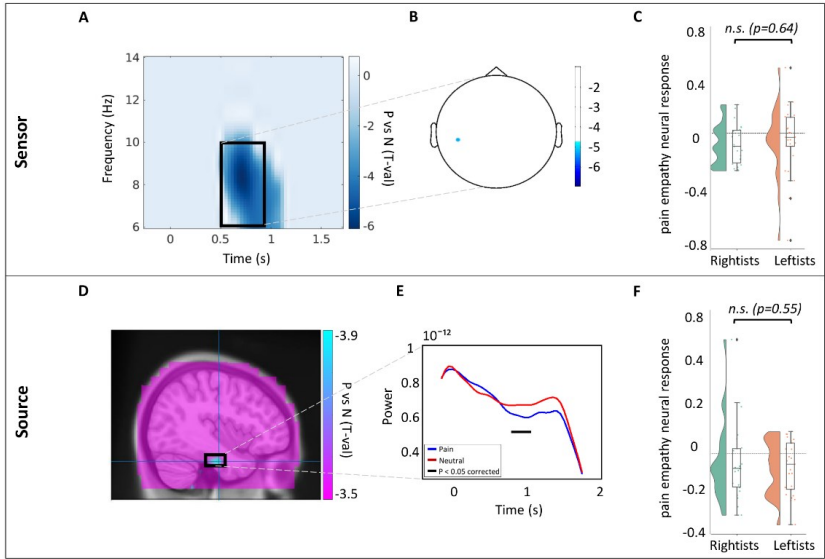
To inspect the source of brain activities during physical pain empathy, we examined sensor and source analysis on each dataset separately. This was necessary due to the different number of sensors in the MEG machines utilized in Finland and Israel.

For the dataset collected in Israel, the sensor analysis in the alpha range revealed a significant alpha suppression (negative  $P_{\text{cluster-cor}} < 0.001$ ,  $T = -5.4$ , permutation test) in the TF window of 7-11 Hz and 600-850 ms (Figure 12A). The peak sensor illustrated in Figure 12B was detected by averaging over the selected TF window. Subsequently, we examined this contrast between the groups at the sensor level (Figure 12C), which was not significant ( $p = 0.69$ , independent T-Test). To examine the source of activity, beamforming analysis was conducted on the selected TF window (peak = 9 Hz) and 5% regularization. The significant source was detected at the right inferior temporal cortex (negative  $P_{\text{cluster-cor}} = 0.004$ ,  $T = -3.5$ , permutation test), represented in Figure 12D. As illustrated in Figure 12E, the VC analysis on the peak coordinate, indicated a significantly greater suppression in response to physical pain compared to neutral stimuli (negative  $P_{\text{cluster-cor}} = 0.012$ ,  $T = -3.1$ , permutation test). Similar to the sensor level, the source level difference in source results between rightists and leftists was insignificant ( $p = 0.11$ , independent T-Test), as shown in Figure 12F.



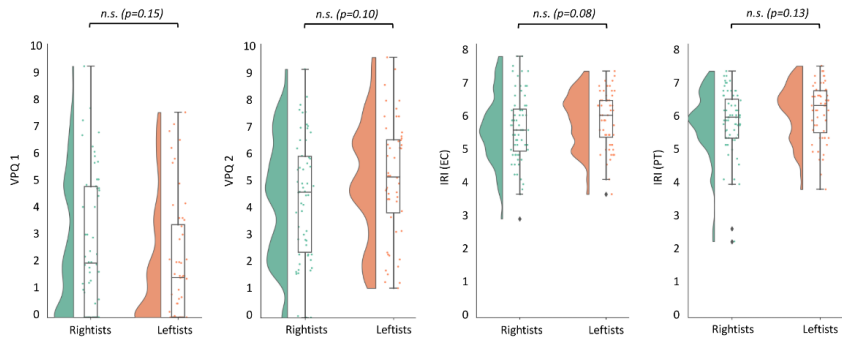
**Figure 12.** A) TFR contrast between the two conditions on 77 subjects. B) Topographic representation of the most suppressed sensor. C) raincloud histogram, indicating the alpha power change ratio of the peak sensor in each political group. D) Sagittal view of alpha suppression peak source in the brain, detected by beamforming technique. E) Temporal changes of the alpha power on peak source for pain (red) and neutral (blue) conditions, indicating VC power ratio in each political group. F) raincloud histogram, indicating pain empathy neural response in each political group.

For the Finnish dataset, the sensor analysis ( Figure 13A), represents a significant decrease in alpha power (negative  $P_{\text{cluster-cor}} = 0.006$ ,  $T = -5.9$ , permutation test). Figures 13B and 13C indicate the peak sensor for the averaged TF window and the power contrast between the two conditions in this peak sensor for subjects in each political group ( $p = 0.64$ , independent T-Test). As represented in Figure 13D, the alpha suppression emanates from the source at the left inferior temporal region (negative  $P_{\text{cluster-cor}} = 0.08$ ,  $T = -4.85$ , permutation test). The result is close to significant and without regularization, and thus should be considered with caution. Further VC analysis on the peak source coordinate indicated a significantly greater suppression in pain versus neutral conditions (negative  $P_{\text{cluster-cor}} = 0.012$ ,  $T = -2.65$ , permutation test), as shown in Figure 13E. Finally, similar to the sensor level results, Figure 13F indicates that the difference in source results between individuals in two opposing political groups was statistically insignificant ( $p = 0.55$ , independent T-Test).



**Figure 13.** A) TFR contrast between the two conditions on 47 subjects. B) Topographic representation of the most suppressed sensor. C) raincloud histogram, indicating the alpha power change ratio of the peak sensor in each political group. D) Sagittal view of alpha suppression peak source in the brain, detected by beamforming technique. E) Temporal changes of the alpha power on peak source for pain (red) and neutral (blue) conditions. F) raincloud histogram, indicating VC power ratio in each political group.

Furthermore, the statistical analysis (i.e. independent t-test) on the behavioral and self-reported empathy measures was conducted to investigate the behavioral contrast between rightists and leftists. As indicated in Figure 14, similar to the neural findings, the contrast for none of the VPQ and IRI subscales reached statistical significance.



**Figure 14.** Pain Empathy – the behavioral and self-reported measures. Behavioral (VPQ) and self-reports (IRI) of empathy in the contrasts between the two opposing political groups.

Moreover, by correlating the sensor and source level neural results of all subjects with VPQ and IRI self-reported results, we found a significant correlation between the sensor result and VPQ 2 subscale ( $r = -0.22$ ,  $p \text{ FDR-cor} = 0.02$ ), indicating a relation between sensor neural result and state empathy.

#### 4.4.4 Conclusion

In this study, a significant neural response was detected in the inferior temporal region during the physical pain empathy task. This area previously demonstrated activation during perceiving human body parts and self/other distinctions (Hooker et al., 2010). The neural and behavioral findings revealed no asymmetry in the level of physical pain empathy between the two political groups. This result was consistent across both populations, affirming the generalizability of the outcome beyond a specific political context. The findings of this study along with the findings from Study III, propose that the interplay between empathy and political ideology is more intricate than previously suggested in prior psychological research. This evidence highlights the importance of considering cultural and societal contexts, diverse forms of empathy, and unbiased measurement techniques, such as neuroimaging technique, while evaluating empathetic reactions.

## 5. Discussion

### 5.1 Main findings

The present thesis provided insights into the neural processes involved in empathy and explored their modulation by various factors such as age, political ideology, and subjective experiences. In study I, we examined various aspects of rhythmic neural patterns during pain empathy experience, measured by MEG. By inspecting the activities in a broad time and frequency range, we evaluated the empathy neural response beyond the dualistic affective-cognitive representation. Our investigation revealed multiple patterns generated from various cortical sources in different time windows. Additionally, we detected a link between one neural pattern and self-reported state empathy, representing subjective experiences. These results support the graded neurophenomenological framework to study empathy. In study II, we investigated the functional meaning of alpha rhythm modulation during empathy in adolescents and young adults by assessing brain activities in consecutive sessions of MEG and fMRI. The findings indicated that at the age of approximately 18 years old, there is a shift in the neural mechanisms underpinning empathy, from high-alpha power enhancement to low-alpha power suppression, reflecting a change from functional inhibition to functional activation in specific brain regions. In studies III and IV, we used MEG to evaluate the interplay between political ideology and neural activities associated with empathy toward vicarious emotional suffering and physical pain, respectively. The results of Study III demonstrated alpha-band activity in the TPJ, indicating empathy response to others' emotional suffering. Interestingly, this empathetic neural response was significantly greater in the group with left-wing political ideology compared to the right-wing political ideology. Conversely, the results of Study IV indicated no asymmetry in the neural response associated with physical pain empathy in the inferior temporal region, among the political groups. The outcome of these two studies revealed a complex association between empathy and political ideology, which depends on several factors such as the targeted component of empathy. All in all, these findings indicate that empathy is a dynamic process influenced by several different factors such as age, political ideology and individual disparities. The results of this thesis represent the intricate interplay between the neural response associated with different sorts of empathy and each of these factor, suggesting a comprehensive perspective while studying empathy process in brain. The following three subsections provide a more detailed discussion of each finding.

## 5.2 Multiple patterns generated from various cortical sources during pain empathy experience measured by MEG

In Study I, four neural patterns in response to observing vicarious pain were detected. In agreement with several MEG/EEG studies on empathy (Cheng et al., 2008; Motoyama et al., 2017; Perry et al., 2010; Whitmarsh et al., 2011), an alpha suppression pattern in the sensory region was found (though the source localization effect yielded a statistical trend,  $P_{\text{cluster-corr}} = 0.09$ ), possibly indicating gating sensory information perceived during the empathy task. In addition to this pattern, significant beta suppression and alpha-beta enhancement patterns were observed in the TFR. The source analysis on the beta suppression pattern revealed that it emanated from two distinct sources in the MCC and PCun, respectively. Recent investigations into the functional implications of beta activity suggested the involvement of beta oscillatory activity in the neural processing of cognitive functions (Engel & Fries, 2010). In parallel, fMRI studies on the role of the MCC and PCun in vicarious pain processing have indicated the involvement of the MCC in both self and vicarious pain perception and affective mirroring (Yesudas & Lee, 2015) and the PCun in the processing of cognitive functions such as perspective-taking and mentalizing (Morelli et al., 2014). Thus, the observed suppression of beta-band activity in the MCC and PCun in response to vicarious pain likely represents the affective and cognitive dimensions of empathy, respectively. The source localization of the late alpha-beta enhancement showed that this pattern was generated from the frontal region, specifically OFC (even though the effect yielded a statistical trend,  $P_{\text{cluster-corr}} = 0.09$ ). Several investigations into alpha rhythm indicated a possible inhibitory role of alpha activity when increased during a task (Schubring & Schupp, 2021; Uusberg et al., 2013). Furthermore, alternative research findings demonstrated the involvement of the OFC in emotion regulation by filtering negative affective information coming to the brain (Hooker & Knight, 2006). These pieces of evidence suggest that observed alpha-beta enhancement in OFC reflects an inhibitory control mechanism activated during perceiving vicarious pain. This pattern was negatively correlated with subjective sensitivity to others' pain, indicating that individuals with greater sensitivity to vicarious pain demonstrated reduced inhibitory control in their brains.

## 5.3 The brain mechanisms underlying empathy undergo electrophysiological and functional changes at the age of approximately 18 years old

In study II, examining empathy in two groups of subjects with an average of 20.5 (group A) and 17.6 (group B) with MEG revealed an alteration in neural at the age of approximately 18 years old. In group A, the observed pattern was similar to the outcomes reported in prior studies on adults utilizing EEG/MEG techniques (Cheng et al., 2008; Levy et al., 2018; Whitmarsh et al., 2011). Conversely, no significant alpha suppression pattern was found in group B and instead, a significant high-alpha enhancement pattern was detected. This age-re-

lated alteration is in agreement with former neurodevelopmental studies on empathy (Decety & Michalska, 2010; Levy et al., 2018), although the MEG study by Levy et al. indicated both low-alpha suppression and high-alpha enhancement in the adolescent group (Levy et al., 2018). Recording both alpha-band neural activity (using MEG) and brain hemodynamic responses (using fMRI) enabled the examination of the functional aspects of the neural pattern shift associated with empathy.

The identified region from each modality was utilized to investigate the ROI in the alternative modality. In group A, by conducting the MEG VC analysis on the coordinates detected during fMRI analysis, significant alpha suppression was found in S1 and motor regions, replicating the findings in former MEG and fMRI studies on empathy. Consistent with the "gating by inhibition" hypothesis, this result validates the initial research question regarding the correspondence of alpha power suppression and functional activation in S1 and other cortical regions during pain empathy. Even though, the results of fMRI ROI analysis on the coordinates detected by MEG source analysis did not corroborate this relation. In group B, MEG VC analysis on the coordinates detected during fMRI analysis revealed significant alpha enhancement in PCC and S1 regions. Likewise, fMRI ROI analysis on the peak sources detected by MEG in ACC and PCC represented significantly less functional activity in pain versus neutral conditions. Thus, both analyses revealed a link between alpha enhancement and decreased BOLD activity, indicative of functional inhibition within specific brain areas for the younger subject group during empathy. This result is in agreement with previous findings on the association between alpha enhancement and active inhibition of sensory information or decrease in BOLD signal (Moosmann et al., 2003; Uusberg et al., 2013) and proposes an inhibitory control mechanism during empathy in adolescents, which gradually diminishes in adulthood. As outlined by Levy et al., the alteration in neural empathic response from adolescence to adulthood may signify the maturation in empathic ability (Levy et al., 2018), which based on the current study, occurs around the age of approximately 18 years old.

#### **5.4 The interplay between empathy and political ideology depends on several factors such as the targeted component of empathy.**

In Studies III and IV, we introduced a novel approach to examine the association of empathy and political ideology, by employing neuroimaging techniques, particularly MEG. In Study III, we detected an asymmetry in the level of empathy toward others' emotional suffering in opposing political groups. In this study, the neural marker of empathy to vicarious emotional suffering was detected in the TPJ area, which repeatedly indicated as a brain region associated with TOM and perspective-taking (Lamm et al., 2011). Greater activation was observed in this region in the leftist compared to the rightist group. In contrast, in Study IV, we failed to detect any connection between brain processes associated with physical pain empathy and political ideology. In both datasets of study IV, the neural marker of empathy to vicarious physical pain was detected in the

inferior temporal region, which was shown to be activated while perceiving human body parts as well as during self/other distinctions (Hooker et al., 2010). The difference in the neural mechanism underlying different types of empathy is in agreement with the former findings indicating dissimilar brain networks involved in emotional versus physical pain empathy (Bruneau et al., 2012). This and other studies suggested that the involvement of different empathy components may vary depending on the stimuli eliciting empathic responses (Bruneau et al., 2012; Lamm et al., 2007). In Study III, the stimuli represented vicarious suffering, and participants tried to watch the world from the protagonist's perspective. This capacity or tendency might vary in participants with different ideological foundations and values. For example, studies showed that individuals with left/liberal ideology feel more concern for other's well-being and have a greater tendency to support social equality (Hasson et al., 2018). However, in Study IV, the stimuli represented pain in the protagonist's body part which could enable shared affective and sensory responses in the observer. This type of empathy involves bottom-up processing and is less related to the observer's ideological values.

To our knowledge, no prior research has employed neuroimaging for this purpose and former investigations into the correlation of these two factors mainly utilized self-reported questionnaires to measure empathy. Studies III and IV provided a unique perspective on the intersection of empathic neural responses and political ideology and examined the aspects that were overlooked in former self-reported studies.

## 5.5 Limitations and Future Perspectives

In Studies I, III, and IV, the investigations were conducted by the MEG technique, and the functional role of the neural activity patterns was interpreted based on the former fMRI studies. Yet, it is important to bear in mind that MEG is subject to certain constraints, and employing other techniques such as fMRI in conjunction with MEG in future investigations can enhance the understanding of the functional role of the patterns detected by MEG.

Another consideration that should be taken into account is the cultural-social context in which the studies were conducted. Given that empathy is a social phenomenon, even the same task design might provide dissimilar results in different countries, particularly, in the investigations that involve variables such as political ideology. For instance, the left-right dimension slightly varies across different countries, and in some countries such as the United States, it is substituted by the liberal-conservative dimension. In Study III and part of Study IV, which were conducted in Israel, the ideological values were influenced by the Israeli–Palestinian conflict. Moreover, a cross-national analysis by Malka et al. revealed a greater association between personality traits and social conservatism in countries with ideological constraints (Malka et al., 2014). In another cross-cultural study by Ivancovsky et al., the inhibitory role of culture was detected during the creativity tasks (Ivancovsky et al., 2019). The findings in this cross-cultural study suggested that certain cultural contexts are more stringent

in evaluating ideas, potentially due to restrictive cultural norms. In Study IV, we conducted experiments in two distinct countries to consider the role of societal context in the results. Notably, the neural and behavioral findings demonstrated consistency across Finnish and Israeli populations. Yet, considering the changes both in the stimulus material and cultural background within a subset of the sample size in Study IV compared to Study III, future investigations can explore whether the null finding in Study IV is solely due to using different stimulus material or cultural background also plays a role.

In addition, in interpreting neuroscientific findings, it is important to consider the potential limitations associated with “reverse inference”, as highlighted by Poldrack (Poldrack, 2006). Reverse inference involves the interpretation of brain activity patterns as indicative of a particular cognitive process, such as empathy, and caution should be taken into account to prevent oversimplified assumptions regarding the exclusive association between observed brain activity and complex cognitive function. Even though, as suggested by Poldrack, reverse inference should be regarded as a tool to further enhance the understanding of brain complexities.

Furthermore, It is also important to note that in Studies III and IV, we explored the potential link between political ideology and empathy without indicating causality. Therefore, further studies can investigate the causality to clarify which variable shapes the other one.

Noteworthy, even though we conducted large-sample MEG and fMRI studies in this thesis compared to former investigations into the neural mechanisms underpinning empathy, the sample size is limited compared to previous self-reported studies on empathy. This could be a potential explanation for the absence of a correlation between neural and behavioral findings in some studies.

Finally, it is important to bear in mind that empathy is not a static characteristic but rather a dynamic trait that can be built or promoted through various methods (Hein, Engelmann, et al., 2016; S. G. Shamay-Tsoory & Hertz, 2022; Wagaman & Segal, 2014). A promising approach for future research is to examine various interventions such as positive learning, as suggested by Hein et al. (Hein, Engelmann, et al., 2016), or contact intervention, as indicated by Wagaman et al. (Wagaman & Segal, 2014) to enhance understanding and foster empathy. Another intriguing avenue is to explore the recently proposed adaptive empathy framework proposed by Shamay-Tsoory et al. (S. G. Shamay-Tsoory & Hertz, 2022) to understand the mechanisms through which empathy is modulated based on feedback.

## 6. Concluding remarks

This thesis contributes to further understanding of the neural mechanisms involved in the processing of different empathy tasks, aiming to identify the variables that influence varying levels of empathy across individuals. Former neuroscientific research on empathy has typically overlooked the role of dependent factors such as age, political ideology, or subjective experiences. The findings in the current thesis provided new insights into the existing knowledge of the empathy process in the brain by prompting inquiries regarding this intricate socio-cognitive process, examining its modulation during adolescence and young adulthood, and evaluating whether it is biased by ideological values and prior experiences.



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