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ORIGINAL PAPER

Changes in Prefrontal fNIRS Activation and Heart Rate Variability During Self-Compassionate Thinking Related to Stressful Memories

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Abstract

Objectives The aim of this study was to investigate the effects of self-compassionate thinking (SCT) related to stressful autobiographical memories (SAM) on the prefrontal cortex (PFC) activity and heart rate variability (HRV) parameters in healthy subjects.

Methods A naturalistic paradigm was built with two conditions, SAM followed by SCT. We used functional near-infrared spectroscopy (fNIRS) to measure oxy and deoxyhemoglobin concentration changes in 33 healthy adults (men = 10) with a mean age of 33.24 years (SD = 6.85). Two HRV parameters were also measured during both conditions: the standard deviations of the normal-to-normal (SDNN-HRV) and the high-frequency component of heart rate variability (HF-HRV).

Results During the SAM condition, the left dorsolateral PFC (DLPFC) and the frontopolar area showed a significantly increased oxyhemoglobin concentration compared with the control condition (corrected-$p < 0.01$). During the SCT condition, the frontopolar area showed a significantly increased oxyhemoglobin compared with the control condition (corrected-$p < 0.001$). A significant increase in time-domain SDNN-HRV ($p = 0.002$) during SCT compared with the SAM condition was also observed. An association between the frontopolar area fNIRS signal and the HF-HRV during SAM condition was found (corrected-$p < 0.05$).

Conclusions Our findings suggested that the SAM condition is associated with activity in the left DLPFC and in the frontopolar area, while the SCF is associated with activity in the frontopolar area. The SCT was related to an increase in SDNN-HRV when compared with the SAM condition, and an association between HF-HRV and PFC activity was seen. Our results also suggested that self-compassionate thinking can be an effective emotional regulation strategy.

Trial Registration Clinical Trials NCT03737084.

Keywords Self-compassion · Stress · Near-infrared spectroscopy · Heart rate variability · Prefrontal cortex

Self-compassion can be described as treating oneself with kindness and self-concern when one is experiencing adversity in life (Neff, 2003). Similarly, to compassion towards others, self-compassion involves perceiving our own suffering, generating the desire to alleviate one's suffering, and treating oneself with understanding and concern. According to Neff (2003), self-compassion includes being open to and mindful of personal suffering, being kind towards the self when experiencing suffering, as well as when experiencing suffering as part of human living. Considering the evidence that self-compassion is an effective way to deal with adverse situations (Stellar et al., 2015; Svendsen et al., 2016) and to validate and recognize reappraisal strategy, we believe that this might be considered a strategy for emotional regulation. However, how could we measure self-compassion? One alternative is to evaluate changes in physiological parameters associated with emotional regulation. Among the physiological correlates of emotional regulation reported in published literature, the present study highlights two parameters: activity in the prefrontal cortex (PFC) and heart rate variability (HRV).

The PFC plays a significant role in the higher-level brain functions, which are described as activities that involve some higher order cognition, such as decision-making, attention

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allocation, and cognitive and emotional processing. It is also known to be related to the "top-down" processes when one's behavior is regulated by internal states or intentions (Davidson & Fox, 1982; Miller & Cohen, 2001). There are specific PFC areas with evidence of interaction with cognitive control and emotional regulation. Davidson (2004) showed that the dorsolateral area of the PFC (DLPFC) is primarily related to various cognitive processes, especially to cognitive control. Hutcherson et al. (2012) showed that the DLPFC and ventromedial area are related to cognitive regulation and decision making. The prefrontal-limbic network plays a major role in the processes of cognitive control and emotional regulation. Two areas of this network, the medial frontopolar cortex and the amygdala, were shown to be negatively correlated; that is, the increased activation in the frontopolar cortex is related to a lower activation of the amygdala (Motzkin et al., 2015; Riedel et al., 2019). There is also evidence that induced acute stress is associated with increased activity in the PFC. Schaal et al. (2019) found a significant increase in neural activity of brain regions of the DLPFC and the orbitofrontal cortex. Rosenbaum et al. (2018) found higher activation in the DLPFC, among other areas. As reported by the studies cited, activity in certain regions of the PFC is related to stress as well as to strategies of emotional regulation.

Among the resources available to assess cortical activity, functional near-infrared spectroscopy (fNIRS) is an optical and non-invasive imaging technique. In recent years, technical and methodological advances revealed fNIRS as a powerful tool to investigate the neural correlates of cognitive and emotional processes. One of the advantages of fNIRS is that it allows the measurement of cortical activity in ecological paradigms (Balardin et al., 2017), which turned this tool into a commonly used resource for investigating cognitive and emotional processes. Some studies have successfully used fNIRS to investigate autobiographical memories of real daily situations. In this investigation, participants recall situations from their own lives that are of greater personal significance than the laboratory stimuli (Maguire, 2001; Svoboda et al., 2006). In a study including healthy adults, Compare et. al (2016) evaluated the effect of autobiographical memories (positive and negative) on the PFC activity using fNIRS. As a result, they found that greater PFC activation occurs during recall of negative episodes than during positive episodes.

Heart rate variability (HRV) is the physiological phenomenon of the variation in the time interval between consecutive heartbeats. HRV is a commonly used measure of the autonomic nervous system (ANS) and it has been associated with both cardiovascular and mental health (Thayer et al., 2012). HRV can be measured in both time and frequency domains. Time-domain measures are calculated by examining the segments between heartbeats or normal-to-normal (NN) intervals. One of the time-domain measures commonly used is the standard deviation (SD) of all "normal-to-normal" (equivalent to RR) intervals (SDNN-HRV). Another time-domain measure commonly used is the root mean square of successive heartbeat interval differences (RMSSD-HRV). The widely used frequency domain of HRV includes power in the low-frequency range (LF-HRV; 0.04–0.15 Hz) and high-frequency range (HF-HRV; 0.15–0.4 Hz) measured in ms^2. HRV is a physiological parameter of the person's ability to modulate their response in stressful situations. A recently published systematic review evaluated the evidence of HRV as a biomarker of top-down self-regulation and found that greater HRV was related to better top-down self-regulation (Holzman & Bridgett, 2017). Lower levels of HRV are an indicator of autonomic dysregulation and they are related to cardiovascular problems, also they have been associated with lower performance on cognitive tasks (Elias & Torres, 2017).

Some studies have evaluated the relationship between self-compassion and HRV. Higher levels of trait self-compassion correlate positively with higher HRV, which indicates that it is associated with a better capacity to regulate emotional responses (Svendsen et al., 2016). Stellar et al. (2015) demonstrated that compassion elicits significant changes in the ANS by increasing activation of the *vagus* nerve, which might facilitate support-giving and care-taking behaviors. Luo et al. (2018) studied the effects of self-compassion on physiological stress response under experimental conditions and found that self-compassionate individuals showed higher HRV at baseline. In a recent study, Luo et al. (2020) investigated the effects of self-compassion on experimental pain, and this study demonstrated that a compassionate self-talk protocol followed by experimental cold pain resulted in an increase in the HRV high-frequency parameter (HF-HRV) and this parameter was associated with lower pain ratings.

Recently, some studies have shown evidence of the association between PFC regions and HRV parameters. Chand et al. (2020) observed an association between HRV and brain networks including cortical regions such as the ventromedial PFC. Prefrontal cortex activity is also related to changes in HRV parameters via the mediation of the cortico-subcortical pathways that modulate the parasympathetic and sympathetic nervous systems (Nikolin et al., 2017). HRV parameters are linked to the performance of executive functions and emotional processing by the PFC (McCraty & Shaffer, 2015; Shaffer & Ginsberg, 2017). Lane et al. (2009) observed that cognitive control had definable neural substrates that correlated with the HF-HRV. In a study that investigated diet self-control, Maier and Hare (2017) found that SDNN-HRV was related to greater activation in the ventromedial PFC. These authors also suggested that HRV might contribute as both an accessible and a robust biomarker for self-control parameters.

As previous studies suggested that there are PFC and HRV correlates of emotional regulation, they can be important targets to evaluate self-compassionate thinking as an emotional regulation strategy. Therefore, the development of a study to investigate these correlates may substantially contribute to the understanding of the physiological processes involved in self-compassionate thinking (SCT). In this sense, we built a naturalistic paradigm containing two conditions: In the first one, the participants were induced to experience their chosen stressful autobiographical memories (SAM), and in the second condition, they were instructed to focus on SCT. Similar paradigms with emotional contrast have been reported in the published literature. A recent study by Kim et al. (2020) evaluated biological markers of compassion using fMRI and HRV. They built a paradigm using two conditions: critical thinking (self-criticism) and self-reassurance (compassionate thinking).

In this study, we sought to build an experimental paradigm to investigate cortical activity and HRV during compassionate thoughts from a more authentic "ecological" experience. In this sense, the SAM condition was developed and used to recall stressful and painful experiences, allowing sub-sequential evaluation of compassionate thoughts related to these recalled situations of suffering. Therefore, the SAM condition contextualized the SCT condition. This paradigm also allows a direct contrast between the SAM and SCT conditions. The aim of the present study was to investigate the effects of SCT related to SAM on the PFC activity, SDNN-HRV, and HF-HRV parameters in healthy subjects. Based on previous findings (Compare et al., 2016; Elias & Torres, 2017; Lane et al., 2009), our hypotheses are as follows: (1) SCT after SAM can decrease the level of cortical activity; (2) SCT related to SAM can increase SDNN-HRV and HF-HRV; and (3) there is an association between PFC activity and HRV parameters (SDNN-HRV and HF-HRV) in both conditions.

Method

Participants

Students and staff from health research and educational institution were invited to participate in the study. Thirty-three healthy adults (men = 10) signed an informed consent form before entering in the study. Participants' mean age was 33.24 years (SD = 6.85). The study was approved by the hospital ethical review committee. The inclusion criteria were to be right-handed, not have a diagnosis or be under treatment for heart disease, and do not have a history of psychiatric illness or neurological disorder. Individuals did not receive any monetary compensation for participation. The study was conducted in accordance with ethical standards for experiments with human volunteers (see also the Declaration of Helsinki, BMJ, 1991; 302, 1194).

Procedures

The researcher described the study to the participants and, after they signed the informed consent, the experiment with fNIRS was carried out. Participants wore the fNIRS cap and were sat down in a comfortable chair in a room with the lights turned off lights and a low level of external light. During the experiment, they were instructed to keep their eyes closed while listening to an audio with instructions for each condition. They were also instructed to avoid any head and body movements.

The experiment followed a block design with two conditions: stressful autobiographical memories (SAM) and self-compassionate thinking (SCT). The audios of each experimental condition lasted for 45 s, followed by a control audio lasting for 25 s. There was a single audio for each condition that was repeated five times, alternating experimental and control conditions (Fig. 1). The audios of each condition were recorded with the following sentences (with time intervals of 5 to 7 s between sentences):

> SAM: "Now try to bring to your mind a recent situation of suffering experienced, try to remember the details of the situation, whether you felt pain, frustration or another feeling, then bring those memories to your mind, remember how you felt in the situation."
> SCT: "Repeat internally by trying to feel each sentence, may I accept my suffering with kindness, may I recognize that suffering is part of life, may I be kind and loving to myself, may I be free from pain and suffering, may I be at peace and be happy."

The instructions for the control condition presented the following phrases (without pauses between phrases): control condition, "Now, let's take a break; stay in your natural state; try to disengage from any task; stay alert with your eyes closed; let your thoughts flow without thinking about anything specific." The two experimental conditions were performed in sequence with an interval of 5 to 10 min between stressful autobiographical memories and self-compassionate thinking conditions.

Measures

fNIRS recording The fNIRS data were acquired using a NIRSport system (NIRx Medical Technologies, Berlin, Germany), with an 8 × 7 PFC layout and a total of 20 channels (Fig. 2). Two wavelengths were used: 760 and 850 nm.

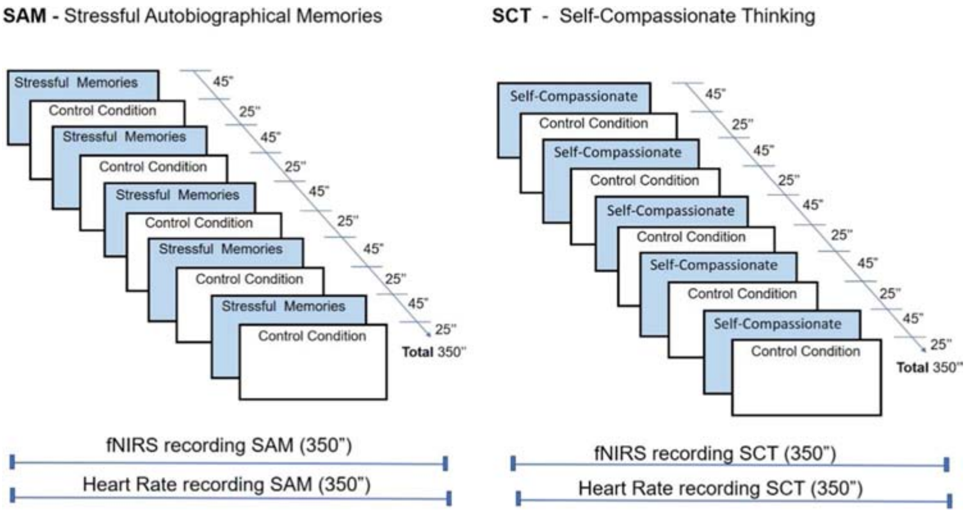

Fig. 1 Experimental design

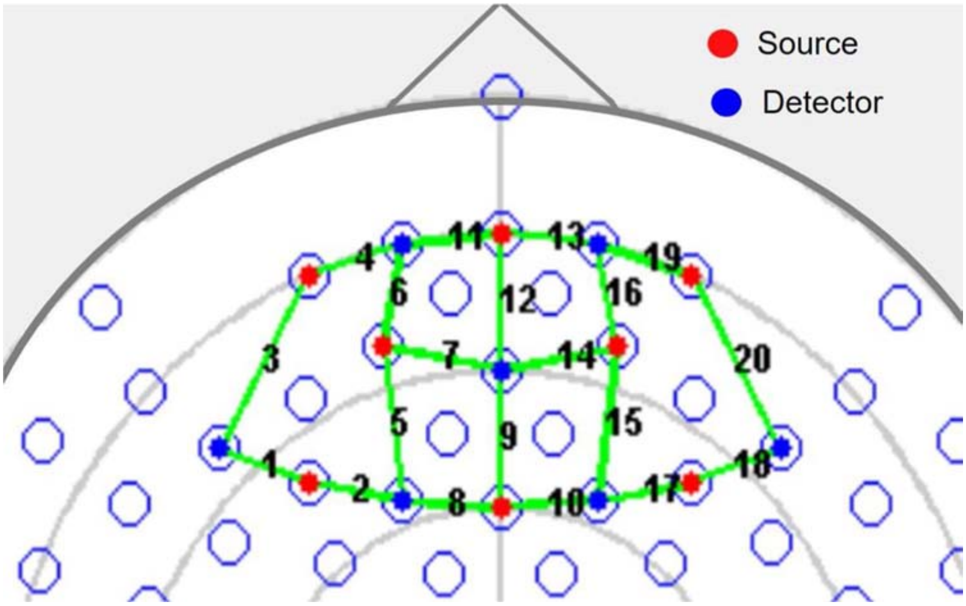

Fig. 2 Probe layout map

The probe comprised 8 LED light-source positions and 7 SiPD detectors mounted on a fabric cap (EASYCAP GmbH, Herrsching, Germany). The fNIRS cap with the optodes was carefully placed on the forehead of participants and they were worn throughout both experimental blocks. Participants wore an overcap to minimize ambient light from reaching their scalp during the test procedure. Figure 2 shows the topographic probe layout map in the standard EEG 10/20 coordinate system (open circles).

The fOLD toolbox (Morais et al., 2018) was used to describe the functional brain regions covered by the optode layout used in our study. This toolbox provides an estimate of the spatial mapping between electroencephalography (EEG) 10/20 system and the brain areas derived from different atlases. Based on this method, the main regions sampled in our study are portions of the dorsolateral prefrontal cortex (Brodmann areas 9 and 46), frontopolar cortex (Brodmann area 10), orbitofrontal cortex (Brodmann area 11), according to the Broadman atlas (Rorden & Brett, 2000; Table 1).

Heart rate recording Cardiac data were also acquired during the experiment with fNIRS using a Polar RS800 monitor (Polar Electro, Finland) in beat-to-beat (RR) mode. Two independent recordings were collected, one during SAM condition and another during SCT condition. Each recording lasted 350 s (approximately 6 min). The data were collected at approximately the same time of day for all participants, between 9:30 a.m. and 12:00 p.m., in order to control circadian effects.

Table 1 Functional brain regions target by the optode layout

Channel	Probe location		Probe location		Brodmann area
	Source	10–20 map	Detector	10–20 map	
C – 1	S1	F3	D1	F5	46 – Left DLPFC
C – 2	S1	F3	D2	F1	09 – Left DLPFC
C – 3	S2	AF7	D1	F5	46 – Left DLPFC
C – 4	S2	AF7	D2	Fp1	10 – Left frontopolar
C – 5	S3	AF3	D2	F1	09 – Left DLPFC
C—6	S3	AF3	D3	Fp1	10 – Left frontopolar
C – 7	S3	AF3	D4	Afz	10 – Left frontopolar
C – 8	S4	Fz	D2	F1	09 – Left DLPFC
C – 9	S4	Fz	D4	Afz	09 – DLPFC
C – 10	S4	Fz	D5	F2	09 – Right DLPFC
C – 11	S5	Fpz	D3	Fp1	10 – Left frontopolar
C – 12	S5	Fpz	D4	Afz	10 – Frontopolar
C – 13	S5	Fpz	D6	Fp2	10 – Right frontopolar
C – 14	S6	AF4	D4	Afz	10 – Right frontopolar
C – 15	S6	AF4	D5	F2	09 – Right DLPFC
C – 16	S6	AF4	D6	Fp2	10 – Right frontopolar
C – 17	S7	F4	D5	F2	09 – Right DLPFC
C – 18	S7	F4	D7	F8	46 – Right DLPFC
C – 19	S8	AF8	D6	Fp2	10 – Right frontopolar
C – 20	S2	AF7	D1	F5	46 – Right DLPFC

Data Analyses

fNIRS Data Analysis Preprocessing and activation analyses were carried out using the NIRS Brain AnalyzIR toolbox (Santosa et al., 2018). As the raw data measured from fNIRS is the voltage related to the detection of each wavelength in each channel, a few pre-processing steps are used to estimate the relative changes in oxy and deoxyhemoglobin concentrations. As preprocessing steps, the missing points (saturation) in raw data were linearly interpolated. After that, the data were converted in sequence to optical density and to the concentration of oxyhemoglobin (HbO) using the modified Beer-Lambert law with an age-adjusted differential path length (Scholkmann & Wolf, 2013), assuming 3 cm distance among optodes. The modified Beer-Lambert Law takes into account the scattering of light in the tissue, which changes with age, and provides an estimate of relative concentrations (in relation to a baseline period) of chromophores (in this case, oxy and deoxyhemoglobin). To evaluate the changes in the brain signal related to the tasks performed in each experimental condition, an autoregressive iterative least-squares model was used to calculate the general linear model (GLM) taking into account the fNIRS physiological noise (Barker et al., 2013). For this method, the usual frequency pre-filtering of physiological noise prior to GLM is not recommended (Huppert, 2016); therefore, the data was not pre-filtered. In the subject-level GLM, the canonical hemodynamic response function was convolved with a boxcar function based on the block design. By doing this, we could evaluate which channels presented a signal variation that would be in line with the hemodynamic response evoked by the task periods, and by identifying the regions that are related to the task. This GLM analysis also included the discrete cosine transform as a high-pass filter to attenuate the effects on frequencies below 0.014 Hz (periods longer than the 70 s period, task + baseline period). The group-level statistics were calculated using the linear mixed effect model with the conditions as fixed effects. Separate group-level models were used to estimate the average signal in each condition (in each model, only the data for the specific condition being evaluated were used). The association between HRV and cortical activity was calculated by adding the SDNN-HRV and HF-HRV separately as a covariable (one covariable at a time) in the mixed effect model for the group level. Also, a group analysis including data from both conditions, accounting for repeated measures, was used to compare SAM condition and SCT condition. Given the number of channels on evaluation, a false discovery rate (FDR) corrected-*p* threshold of 0.05 was adopted to define significant results in each group-level analysis.

Heart Rate Data Analysis In order to calculate the HRV parameters, cardiac data were exported as a text file to the Kubios HRV 2.0 software (The Biomedical Signal and Medical Imaging Analysis Group, University of Kuopio, Finland). This software complies with guidelines for measurement of

HRV recommended by the Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology (1996). According to the Task Force recommendations, the duration of recordings should be standardized. In this sense, short-term 5-min recordings and 24-h long-term recordings seem to be appropriate options. In our study, the total recording time was 350 s (duration of each condition) and the last 300 s (5 min) of each recording was analyzed to ensure the stability of heart rate (HR) data, and follow the short-term standard duration. HRV can be evaluated in both time- and frequency domains. We choose to use one HRV measure of time-domain and one HRV measure of frequency-domain. The time-domain methods are the simplest to perform since they are applied straight to the series of successive RR interval values. The interbeat intervals or RR intervals are obtained as differences between successive R-wave occurrence times. In this study, we adopted the standard deviation of all "normal-to-normal" intervals (SDNN-HRV) as our time-domain measure of variability, since it has been reported to be least compromised by different data preprocessing pipelines, less affected by editing, especially regarding the application of artifact correction (Salo et al., 2001). The SDNN-HRV expresses the overall (both short-term and long-term) variation within the RR interval series. However, in the 5-min settings, the SDNN provides more information about shorter cycles (higher frequency variations) (Task Force of the European Society of Cardiology & the North American Society of Pacing & Electrophysiology, 1996). A power spectrum density (PSD) estimate was calculated for the RR interval series as the frequency-domain method. The RR interval series was converted to an equidistantly sampled series by a cubic spline interpolation prior to PSD estimation. A fast Fourier transform (FFT) with Welch's method was used for the PSD estimation (Tarvainen et al., 2014). The generalized frequency bands in the case of short-term HRV recordings are the very low frequency (VLF, 0–0.04 Hz), low frequency (LF, 0.04–0.15 Hz), and high frequency (HF, 0.15–0.4 Hz). The high-frequency (HF) component (0.15–0.40 Hz) was used as our estimate of the HRV frequency domain. We opted to use HF-HRV because it is widely recognized as a measure of ANS activity, and it is also associated with emotional regulation and self-compassion (Allen et al., 2015; Lane et al., 2009; Luo et al., 2018).

Paired t-tests were used for within-group comparisons for the two blocks: stressful autobiographical memories and self-compassionate thinking. For this analysis, the JASP software, version 0.9.1 (www.jasp-stats.org), was used. An alpha level of 5% ($p < 0.05$) was used as a threshold for significant effects.

Results

Neural Activity Contrast Between Experimental Conditions vs Control Condition

When comparing the stressful autobiographical memory condition with the control condition, we found five channels with significant activity based on oxyhemoglobin (oxyHb) concentration. Channels 3, 5, and 6 in the left DLPFC, channel 4 in the left frontopolar area, and channel 12 in the central frontopolar area showed significantly increased oxyhemoglobin concentration (oxy). Based on deoxyhemoglobin (deoxyHb), the difference between stressful autobiographical memory condition and control condition was significant only in channel 12 in the frontopolar area (see Table 2 and Fig. 3).

When comparing the self-compassionate thinking condition with the control condition, we found only one channel with significant activity (Table 3). Channel 7, in the left frontopolar area, showed significantly increased oxyhemoglobin concentration and also showed a significant decrease in deoxyhemoglobin concentration (Fig. 3).

Comparison Between Stressful Autobiographical Memories and Self-Compassionate Thinking

When comparing the stressful autobiographical memories with the self-compassionate thinking (linear model including both conditions, accounting for repeated measures, and comparing the estimated beta-values for each condition), we found three channels with significant

Table 2 Channels with significant activity during stressful autobiographical memories condition, showing Student's *t*-test values, *p* values, and for corrected-*p* values

Hemoglobin	Channel	T	*p*	Corrected *p*	Brodmann area
oxyHb	3	2.95	0.005	**0.038**	46 – Left DLPFC
	4	5.46	< 0.001	**< 0.001**	10 – Left frontopolar
	5	3.81	< 0.001	**0.005**	09 – Left DLPFC
	6	3.38	0.002	**0.015**	10 – Left frontopolar
	12	6.68	< 0.001	**< 0.001**	10 – Frontopolar
deoxyHb	12	– 3.95	< 0.001	**0.002**	10 – Frontopolar

Significant values ($p < 0.05$) are in bold

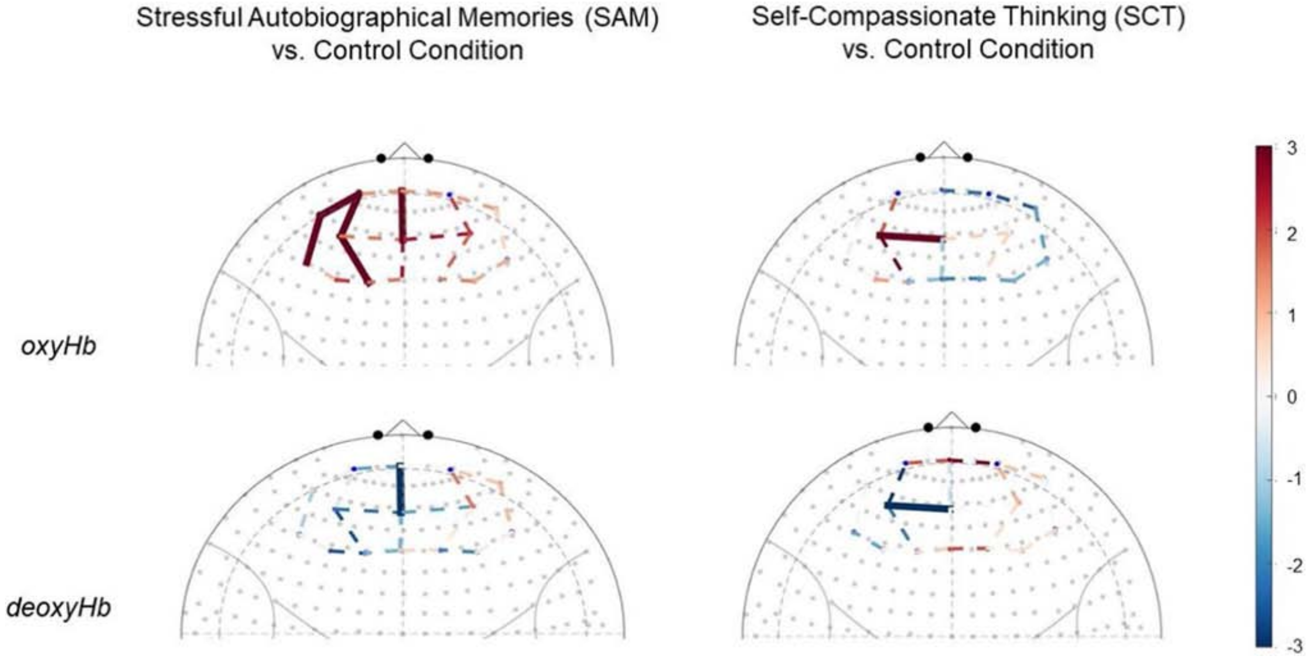

Fig. 3 Neural activity contrast in each experimental condition vs. control condition. The color of each line (channel) refers to the t-values associated with the change in oxyhemoglobin (top) and deoxyhemoglobin (bottom) between each condition and resting state (control condition), as shown on the scale of − 3 to 3. Continuous lines indicate significant differences and dashed lines indicate non-significant differences

Table 3 Channel with significant activity during self-compassionate thinking, showing Student's t-test values, *p* values, and for corrected *p*-values

Hemoglobin	Channel	T	*p*	Corrected *p*	Brodmann area
oxyHb	7	4.12	< 0.001	**< 0.001**	10 – Left frontopolar
deoxyHb	7	− 3.28	0.003	**0.05**	10 – Left frontopolar

Significant values ($p < 0.05$) are in bold

Table 4 Channels with significant activity when we compared stressful autobiographical memories > self-compassionate thinking, showing Student's t-test values, *p* values, and for corrected *p* values

Hemoglobin	Channel	*T*	*p*	Corrected *p*	Brodmann area
oxyHb	4	4.06	< 0.001	**0.004**	10 – Left frontopolar
	9	3.04	0.003	**0.034**	09 – DLPFC
	12	3.94	< 0.001	**0.004**	10 – Frontopolar
deoxyHb	2	− 3.03	0.003	**0.034**	09 – Left DLPFC

Significant values ($p < 0.05$) are in bold

activity in oxyhemoglobin and one in deoxyhemoglobin (Table 4). One channel in the left frontopolar area (channel 4) and two channels in the central frontopolar area (channels 9 and 12) showed significantly increased levels of oxyhemoglobin concentration. One channel in the left DLPFC (channel 2) showed significantly decreased levels of deoxyhemoglobin concentration during the stressful autobiographical memories condition when compared to self-compassionate thinking (Table 4; Fig. 4).

HRV During Each Experimental Condition

When we compared the HRV during both experimental conditions, stressful autobiographical memories (SAM)

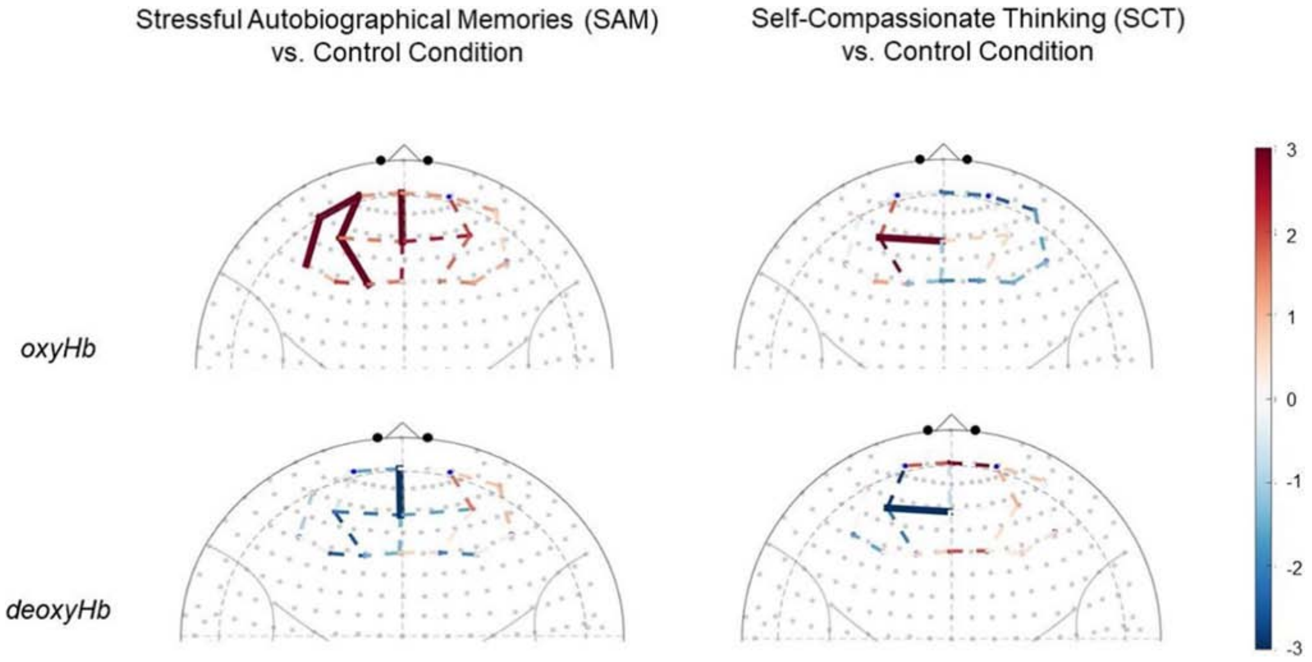

Fig. 4 Stressful autobiographical memories > self-compassionate thinking. The color of each line (channel) refers to the t-values associated with the change in oxyhemoglobin (right) and deoxyhemoglobin (left) between the two conditions, as shown on the scale of − 5 to 5. Continuous lines indicate significant differences and dashed lines indicate non-significant differences

Table 5 Descriptive statistics: age (years); *HR*, heart rate; *SDNN*, standard deviation of all NN intervals; *HF*, high-frequency; *SAM*, stressful autobiographical memories; SCT, self-compassionate thinking

Descriptive statistics		SAM			SCT		
	Age	HR	SDNN	HF	HR	SDNN	HF
Mean	32.24	92.42	91.76	3397	90.90	104.40	4200
St. deviation	6.856	17.67	62.45	5662	21.11	70.43	5157
Minimum	21.00	62.00	18.00	104	62.00	13.00	38
Maximum	46.00	130.0	219.0	25,828	130.00	238.00	18,061

Table 6 Student's t-test for paired samples. *HR*, heart rate, *HF*, high frequency; *SDNN*, standard deviation of normal-to-normal intervals between experimental conditions: stressful autobiographical memories (SAM) and self-compassionate thinking (SCT). *Df*, degrees of freedom

	SAM	SCT	*t*	Df	*p*	Cohen's d
HR	92.42 (±17.67)	90.90 (±21.11)	0.808	32	0.425	0.141
SDNN	91.76 (±62.45)	104.4 (±70.43)	− 3.308	32	**0.002**	− 0.576
HF	3397 (±5662)	4201(±5157)	− 0.959	32	0.345	-0.167

Significant values ($p < 0.05$) are in bold

and self-compassionate thinking, the results showed an increase in HRV ($p = 0.002$) during self-compassionate thinking (SCT) (Tables 5 and 6). The heart rate (HR) variation between the conditions was not significant (Fig. 5).

Association Between Cortical Activity and HRV (SDNN and HF) During Each Condition

The analyses performed to assess the relationship between the HRV variables and the hemodynamic response in SAM condition (Table 7 and Fig. 6) revealed a significant association between SDNN and deoxyhemoglobin in fNIRS channel 16 in the right frontopolar cortex. Furthermore, a significant association between HF and deoxyhemoglobin was found in three fNIRS channels (6, 7, and 16) in the left and right frontopolar cortex. HF was also related to oxyhemoglobin in channel 7 during the SAM condition in the left frontopolar cortex. No associations were found in the SCT condition.

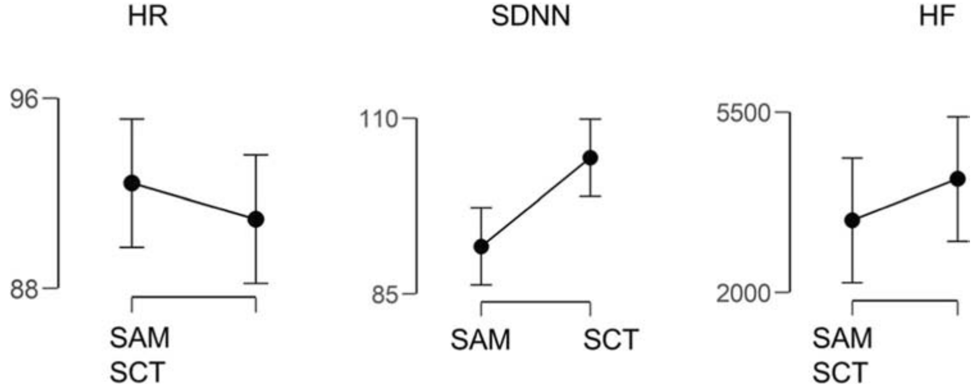

Fig. 5 Paired t-tests, heart rate (HR), standard deviation of normal-to-normal intervals (SDNN), and high frequency (HF) within-group comparisons for the two conditions: stressful autobiographical memories (SAM) and self-compassionate thinking (SCT)

Table 7 Channels with significant association between stressful autobiographical memories (SAM) condition and the HRV parameters (SDNN and HF). Showing Student's t-test values, *p* values, and for corrected-*p* values

Condition	Hemoglobin	Channel	t	*p*	Corrected *p*	Brodmann area
SAM vs SDNN	deoxyHb	16	3.22	0.003	**0.043**	10 – Right frontopolar
SAM vs HF	oxyHb	07	3.61	0.001	**0.015**	10 – Left frontopolar
	deoxyHb	06	− 3.54	0.002	**0.014**	10 – Left frontopolar
	deoxyHb	07	− 4.89	< 0.001	**0.001**	10 – Left frontopolar
	deoxyHb	16	3.94	< 0.001	**0.004**	10 – Right frontopolar

Significant values ($p < 0.05$) are in bold

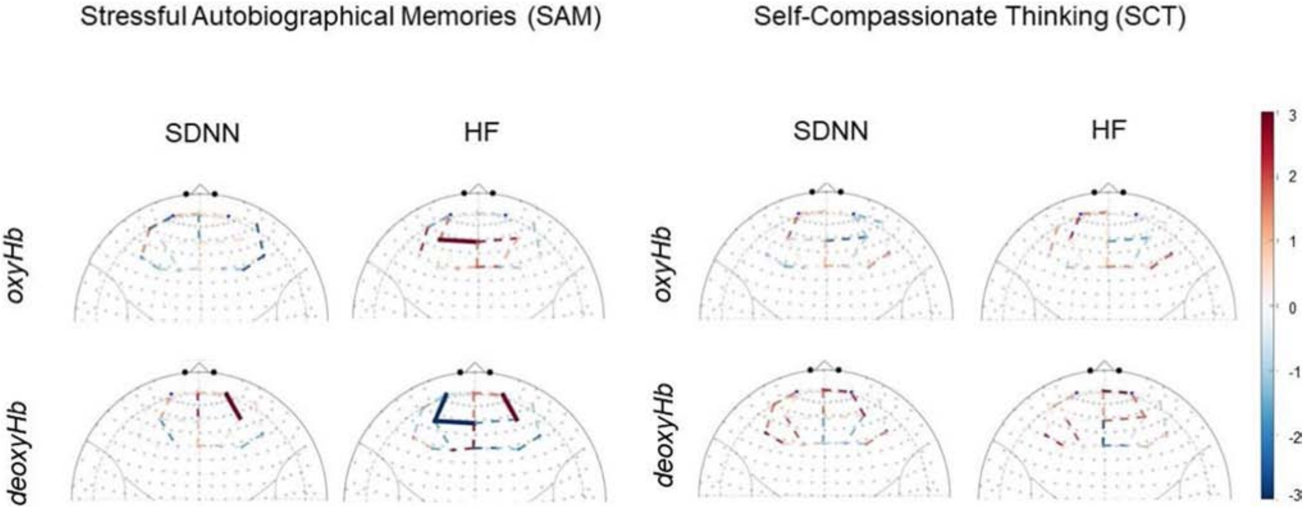

Fig. 6 Association between cortical activity and HRV (SDNN and HF). The color of each line (channel) indicates the t-values associated with the change in oxyhemoglobin (oxyHb) and deoxyhemoglobin (deoxyHb) between each condition and HRV parameters (SDNN and HF), as shown on the scale of − 3 to 3. Continuous lines indicate significant differences and dashed lines indicate non-significant differences

Discussion

The aim of this study was to investigate the effects of self-compassionate thinking related to stressful memories on the PFC activity (using fNIRS) and HRV parameters in healthy subjects. The results suggested that self-compassionate thinking can increase SDNN-HRV as well as decrease cortical PFC activity in relation to the stressful memories condition. We found a significant correlation between cortical activity and high-frequency component of HRV (HF-HRV) during stressful memories. Moreover, we showed that the ecological paradigm developed for this study was able to identify changes in PFC activation and HRV during self-compassionate thinking related to stressful memories.

Firstly, we accessed the cortical activity during stressful memories and self-compassionate thinking, separately. During the stressful autobiographical memories, we found that four channels (3, 4, 5, and 6) in the left PFC (predominantly in the left DLPFC), and channel 12 in the central frontopolar area showed significantly increased oxyhemoglobin concentration than the control condition. Channel 12 also showed decreased deoxyhemoglobin concentration and demonstrated a coherence with the oxyhemoglobin findings. On the other hand, during the self-compassionate thinking condition, we found that only channel 7 in the frontopolar cortex showed significant and coherent changes in oxyhemoglobin (increased) and in deoxyhemoglobin (decreased) concentrations compared with the control condition.

During stressful memories, a greater number of active channels was observed, with a predominance of the left hemisphere and one channel in the frontopolar region. These results are consistent with the pattern found in autobiographical memory studies. In a review including 11 studies using autobiographical memories tasks and hemodynamic imaging techniques, Maguire (2001) reported a greater activation in the left hemisphere and in the medial brain areas. These areas included the temporopolar cortex, medial temporal regions, medial prefrontal cortex, among others. The left-lateralized pattern may reflect the initial search process of general autobiographical knowledge, as proposed by Conway et al. (2001). Alternatively, the left DLPFC activation was also observed in other contexts. Li et al. (2017) carried out a study to investigate the neural correlates of cognitive flexibility in children, using fNIRS and Stroop task. They found that left DLPFC activation was associated with cognitive flexibility, during a self-referential task that requires cognitive effort, a finding that was similar to the processing expected in the SAM condition. Likewise, the studies by Schaal et al. (2019) and Rosenbaum et al. (2018) found significantly increased neural activity of the DLPFC, among other regions, during an induced stress task.

When we directly compared the condition of stressful memory with self-compassionate thinking, the first presented greater activity in the PFC. Thus, the results found in the present study seem to confirm our first hypothesis, that is, compassionate thinking is associated with a decrease in PFC activity, when compared with the stressful memories condition. A similar result was also found by Compare et al. (2016), who evaluated the effect of autobiographical memories (positive and negative) on the PFC activity using fNIRS. In that study, they observed that greater PFC activation occurs during the recall of negative episodes in relation to the positive episodes. This may happen due to negative episodes such as stressful memories, which require greater cognitive demand during the task and consequently greater activation in the PFC. This might explain the result found in our study as in the SAM condition there is a greater cognitive demand in the processing of stressful memories in relation to the SCT. The results of the present study corroborate with previous studies and contribute to clarifying the role of PFC in the processing of negative memories and in the development of emotional regulation strategies.

In both conditions of our study, we found significant activation in the Brodmann area 10, a region strongly associated with self-referential processing and considered a central factor of autobiographical memory (Johnson et al., 2002). This finding demonstrates a coherence between our study and previous findings, since in both conditions, whether SAM or SCT, there is a self-referential component. We argue that compassionate thinking is an adaptive way of thinking about stressful situations and this can be considered a kind of reappraisal approach. According to the findings of Ochsner et al. (2002), reappraisal is associated with an increase in activity in the lateral and medial prefrontal regions (Brodmann area 10), and to a decrease in the activity of the amygdala. These results also agree with previous findings and support the hypothesis that the prefrontal cortex is involved in cognitive strategies that can modulate activity in multiple emotion processing systems (Miller & Cohen, 2001; Motzkin et al., 2015).

The results of the HRV comparison between the two conditions demonstrated that, during self-compassionate thinking, there was a significant increase in HRV parameters in relation to stressful memories. The time-domain parameter SDNN-HRV showed a statistically significant increase, while the frequency-domain HF-HRV did not. Cohen's d suggests a very small or no effect related to change in HF-HRV, despite being in the same direction of the effect that the SDNN-HRV (higher HRV in the SCT condition). This could be explained due to our sample size limitation. Alternatively, the SDNN-HRV could be a more sensitive metric, as it reflects both sympathetic and parasympathetic activity, while HF-HRV is more related to parasympathetic activity (Shaffer & Ginsberg, 2017).

There are some studies in the literature showing a positive correlation between self-compassion and HRV parameters, using self-reported scales in general. Svendsen et al. (2016) showed that individuals with greater trait self-compassion have higher levels of HRV. Luo et al. (2018) demonstrated that self-compassionate individuals showed higher HRV and reported lower negative effects in response to stress, highlighting the role of self-compassion in the adjustment of physiological and psychological responses to stress. Other studies have assessed the effect of self-compassion-based interventions on HRV, indicating that such interventions improve HRV parameters: Petrocchi et al. (2017) tested whether a mirror could enhance the efficacy of self-compassion manipulation on HRV. In that study, eighty-six participants who repeated compassion-focused phrases while looking at the mirror reported higher levels of HRV, according to the method described in Gilbert's study (2010). More recent studies continue to corroborate and expand knowledge about the relationship between compassion and HRV parameters. The study of Luo et al. (2020) investigated the effects of a compassionate self-talk protocol on experimental pain and HRV parameters with induction of a compassionate state through phrases similar to the phrases used in our study. They found that compassionate self-talk was associated with an increase in the high-frequency parameter (HF-HRV) in the context of experimental pain. In the same sense, Kim et al (2020) demonstrated that a brief compassionate training was associated with an increased parasympathetic response as measured by an increase in RMSSD-HRV, versus the resting state. In the present study, the observed increase in the SDNN-HRV parameter during the compassionate thinking, related to the stressful memories, partially confirms our second hypothesis and they are in agreement with the studies mentioned above.

Regarding the interaction between PFC activity and HRV parameters, the present study found a significant association between the frontopolar area and the HF component of HRV during the SAM condition. Similarly, during SAM an association was also observed between SDNN and deoxyhemoglobin, although no relation was detected with oxyhemoglobin. These findings are in line with the third hypothesis of our study and, therefore, suggest the existence of an association between HRV and PFC activity.

Previous studies with diverse methods and experimental designs also found similar results (Lane et al., 2009; Maier & Hare, 2017; Nikolin et al., 2017). A likely explanation would be that this association takes place via the mediation of the cortico-subcortical pathways that regulate the parasympathetic and sympathetic branches of the ANS. This interaction is also aligned with the neurovisceral integration model (Park et al., 2013; Thayer & Lane, 2000) in which the cardiac vagal tone, indexed by HRV, can indicate the functional integrity of the neural networks implicated in emotion and cognition interactions. However, we did not find significant associations during SCT. This could be related to higher heterogeneity of mental processes during SCT along with the small sample. Nevertheless, the SAM condition may require more cognitive effort for dealing with stressful memories compared with the SCT condition in which the participants were guided to listen and mentally repeat some compassionate phrases. This hypothesis should be further investigated in future studies.

These findings suggest that PFC activity and HRV parameters might contribute as a non-invasive, accessible, and robust biomarker for emotion regulation investigation. The present study was able to demonstrate the feasibility and practicality of using fNIRS along with HRV parameters for investigating emotional regulation strategies. The results indicated that compassionate thinking has positive effects on HRV parameters (increased SDNN-HRV) and on brain activity measure with fNIRS (decreased PFC activity). Thus, it could be considered an effective emotional regulation strategy in face of stressful memories. These study findings suggested that the use of this experimental design may be adequate to investigate the pre- and post-effects of mind–body interventions such as mindfulness-based programs, compassion-based programs, among others.

Limitations and Future Research

This study included a small sample size and, therefore, might not accurately reflect the general population. It was also limited because we did not control respiratory activity during the experimental measurements. Controlling breathing rate might give additional information, since ambulatory respiratory sinus arrhythmia magnitude is a vagally mediated index of HRV (Grossman & Taylor, 2007). The period of HRV analyzed included the resting state intervals which may have affected the accuracy of the results. However, this limitation was minimized due to the instructions and time of the resting being identical in SAM and SCT conditions. The inclusion of participant reports of the affective valence during experimental conditions would allow greater accuracy in the findings. Another limitation was that the conditions were recorded in different fNIRS runs. Therefore, there might be presentation sequence effects. Additionally, possible noises may affect the hemodynamic response in time. This could limit the accuracy of the comparison between the two experimental conditions. However, this effect was hindered, as both conditions were carried out in one session without cap removal.

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Author Contribution FRMS: designed and executed the study, collected data, composed and edited the manuscript. PRB: analyzed the data and wrote part of the results and discussion. JBB: collaborated with the design of the study. MAA: collaborated with the design of the study. MR: collaborated with the design of the study. SL: collaborated with the design of the study and analyzed part of the data. GLTN: collaborated with the design of the study. EHK: provided supervision, collaborated with the design of the study and writing of the manuscript. All authors read and approved the final manuscript.

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Data Availability The authors will share data from the study upon reasonable request to the corresponding author.

Declarations

Ethics Approval This trial is registered at Clinical Trials: NCT03737084. It was approved by the Ethics Committee in Research of Hospital Israelita Albert Einstein, number: 79179417.4.0000.0071 and follow ethical standards of the Helsinki Declaration of 1964 and its later amendments.

Informed Consent Statement Informed consent was obtained from all participants who participated in the study.

Conflict of Interest Maria Adelia de Aratanha is employed by NIRx Medizintechnik GmbH. Paulo Rodrigo Bazán provides scientific consulting to Brain Support Corporation, which is a distributor of NIRx Medizintechnik GmbH.

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