CATÓLICA
INSTITUTO DE CIÊNCIAS DA SAÚDE

LISBOA·PORTO·VISEU

PAIN ACCURACY: IS THERE A LINK BETWEEN ACCURACY IN PAIN REPORT AND ACCURACY IN INTEROCEPTION AND TASTE TASKS?

Dissertação apresentada à Universidade Católica Portuguesa
para obtenção do grau de mestre em

Neuropsicologia

Por

Mariana Ribolhos Agostinho

Lisboa, 2018

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REPORTAR A DOR COM PRECISÃO: EXISTEM LIGAÇÕES ENTRE A CAPACIDADE DE REPORTAR A DOR E OUTRAS MODALIDADES SENSORIAIS?

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Sob a orientação de Prof.ª Doutora Rita Canaipa e Prof. Doutor Roi Treister

Lisboa, 2018

Abstract

Purpose: Pain intensity, as intensities of other subjective experiences is challenging to measure. The subjective nature of pain assessment and the variability in how patients are understanding and using pain scales are negatively affecting patient-health care provider communication and reducing the essay sensitivity of pain related studies. Little is known about the ability of patients to accurately report pain, and its possible relations with the ability to accurately report other bodily sensations. The aim of this study was to explore the relationships between the ability to accurately report pain and the ability to accurately report other sensations.

Participants and methods: Healthy volunteers enrolled from local universities underwent the FAST procedure, to assess pain reporting accuracy, a taste task, to assess tastes (sweet and salty solutions) intensity reporting accuracy, and the heartbeat perception task, an interoceptive task aimed to assess how accurate subjects are in monitoring and reporting their own heartbeat. In addition, all subjects completed the Multidimensional Assessment of Interoceptive Awareness (MAIA), the Perceived Stress Scale (PSS) and Hospital Anxiety and Depression Scale (HADS). Spearman's correlations were used to assess relations between the accuracy tasks (FAST and taste) and interoception measures (heartbeat task and MAIA), as well associations with pain-related psychological questionnaires (PSS and HADS).

Results: Ability to accurately report the sensations of different modalities were independent of each other ($P>0.05$ for all outcome measures). Positive correlations were found within modality, between reporting accuracy of salt and sweet solutions (Spearman's $r=0.477$, $P<0.001$). No correlations were found between the psychological and accuracy measures.

Conclusion: Pain reporting accuracy is not related to interoceptive awareness of other modalities. Further research is ongoing to investigate the clinical relevance of pain reporting accuracy.

Keywords: Pain assessment, Pain intensity; Interoceptive awareness, Subjective measures

Resumo

Objetivo: A avaliação da intensidade da dor, assim como a avaliação de outras experiências subjetivas tem representado um grande desafio para a investigação. A natureza subjetiva da avaliação da dor e a variabilidade que os doentes revelam na compreensão e utilização de escalas de dor tem tido um impacto negativo na comunicação entre os doentes e os profissionais de saúde, e tem tido consequências na diminuição da sensibilidade dos estudos relacionados com a dor. Pouco se sabe sobre a capacidade que os doentes têm de reportar com precisão a dor e que possíveis relações existem com a capacidade de reportarem com precisão outras sensações.

Participantes e métodos: Foram recrutados participantes saudáveis de universidade locais, a quem foi aplicado um novo procedimento, o FAST, para avaliar a precisão nos relatos de dor, uma tarefa de paladar, para avaliar a precisão nos relatos de intensidades de diferentes gostos (soluções doces e salgadas), e a tarefa de perceção do batimento cardíaco, uma tarefa de interoceção utilizada com o objetivo de avaliar o quão precisos os indivíduos são na monitorização e no relato do seu batimento cardíaco. Para além disto, os participantes preencheram o MAIA (Avaliação Multidimensional da Consciência Interoceptiva), a Escala de Stress Percebido (ESP) e a Escala Hospitalar de Depressão e Ansiedade (HADS). As relações entre as tarefas de precisão (FAST e paladar) e as medidas de interoceção (batimento cardíaco e MAIA), assim como as associações com os questionários de dimensões psicológicas relacionados com a dor (ESP e EHDA), foram analisadas com o coeficiente de correlação de Spearman.

Resultados: As capacidades para reportar de forma precisa as sensações de diferentes modalidades revelaram-se independentes ($P>0.05$ para todas as medidas de resultados). Foram encontradas correlações positivas na mesma modalidade sensorial (intramodalidade) entre a capacidade de reportar com precisão soluções doces e salgadas (correlações de Spearman $r=0.477$, $P<0.001$). Não se encontram correlações entre dimensões psicológicas e medidas de precisão.

Conclusão: A capacidade para reportar a dor com precisão não se relaciona com a consciência interoceptiva de outras modalidades sensoriais. Novos

estudos estão em curso, e são necessários, para melhor compreender a relevância clínica da precisão na avaliação da dor.
Palavras-chave: Avaliação de dor; Intensidade de dor; Consciência interocetiva, Medidas subjetivas.

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1. Literature Revision

1.1 Pain

Pain is a complex phenomenon defined by the International Association for the Study of Pain (IASP) as an “unpleasant sensory and emotional experience associated with actual or potential tissue damage or describe in terms of such damage”. It is a conscious and subjective experience influenced by memories, emotional and cognitive factors. It is considered an experience with high evolutionary value because it guarantees protection from potentially harmful stimulus and situations. Yet in some situations the pain experience can become maladaptive, leading to chronic pain conditions (Pollatos & Critchley, 2012; Wiech & Tracey, 2013; Tracey & Mantyh, 2007).

Chronic pain is currently a huge health problem that affects about one in each five persons and has an estimated prevalence from 19% to 35% across various countries in the world (Breivik, Collett, Ventafridda, Cohen & Gallacher, 2006; Breivik, Eisenberg & O’Brien, 2013; Tracey & Mantyh, 2007). The high prevalence and burden of pain is related to the lack of adequate pain treatments and medication. Despite treatments, many patients suffer from pain, which in turn affect their personal, social and professional lives. The social and economic impact of pain is high (Barham, 2012; Phillips, 2006, 2009).

Pain is influenced by a complex set of factors and scored on scales that are variably understood. It is not surprising, hence, that pain assessment is a real challenge. As in case of any condition, adequate pain treatment relies on accurate assessment of subjects’ pain. It is not only the clinical care that is negatively impacted; clinical research and the development of new treatments are comprised by the high variance of pain.

Many experts in the field of pain agree that analgesic clinical trials often fail because they rely on patient’s pain reports, which reduce the assay sensitivity of these trials (Wager et al., 2004; Dworkin et al., 2012).

One reason contributing to the low statistical power has been attributed to the high variability of the participants’ pain scores (Treister, Eaton, Trudeau, Elder, & P Katz, 2017). As in any other measure, part of this variability is due to true

variance: pain does fluctuate from day to day and even hour to hour, in many patients. Another source of variance is the error variance. This relates to any reason that influence pain ratings. As a subjective experience is difficult to measure, it is susceptible to error due to difficulties in accurately and reliably, conveying the internal pain sensations using common pain scales (e.g. Visual Analogue Scale, Numeric Rating Scale; Loggia, Juneau, & Bushnell, 2011; Treister, et al., 2017).

Pain can be assessed using different methods. Clinical pain, the spontaneous pain that the patients feel can be assessed using self-report questionnaires (e.g. Brief Pain Inventory, MacGill Pain Questionnaire) (Younger, McCue & Mackey, 2009) and behavioural observation. Visual analogue scales and Numerical Pain Rating Scales can also be used to assess spontaneous pain. In these, the subject is asked to rate his pain. In laboratory setting, it is more frequent to study evoked pain. The experimenter induces pain through a mechanical, thermal, electrical o other stimulus modality and the subject report, again on a VAS an NRS the pain felt. Thresholds, tolerance and pain intensity assessments can be performed. The VAS and NRS are either used in the more recent dynamic pain methods, as conditioned pain modulation and temporal summation, known for their ability to assess the activity of pain modulation systems (Kennedy, Kemp, Ridout, Yarnitsky & Rice, 2016; Nahman-Averbuch et al., 2013).

The above methods are all rely on patients reports on rating scales. However, subjects may evidence differences in their pain reporting abilities. Some subjects may report their pain levels reliably, reporting the same pain intensity in response to a specific stimulus, and accurately, in a good approximation to the real experience. Others, may not be good, changing easily their pain reports. In these situations, the individual's evidence high variability in their reports. In clinical trials, this high variability has been related to an increased response in placebo conditions, thus undermining the ability of the essays to demonstrate the effect of analgesics (Harris et al., 2005; Dworkin et al., 2010; Vachon-Presseau et al., 2018). Further studies suggested that there are significant differences between subjects in their pain reporting skills and that selecting good reporting pain subjects in clinical trials can improve assay sensitivity (Harris et al., 2005; Farrar et al., 2014; Treister et al., 2017).

1.2 Focused Analgesia Selection Test (FAST)

In order to characterize the differences in pain reporting abilities, Treister and colleagues (2017), developed the Focused Analgesia Selection Test (FAST), a method aimed to measure patients' pain reporting skills, which discriminates between the "good and poor" reporters. FAST relies on recording subjects' pain reports in response to repeated administration of noxious thermal stimuli of various intensities applied to ventral surface of the subject's non-dominant arm. This method exposes subjects to evoked pain stimuli of known intensities and ask them to rate its intensity. It uses the Medoc® Thermal Sensory Analyzer II incorporating a Peltier element-based thermode (30 x 30 mm^2). Subjects were instructed to rate their perceived pain intensity in response to each stimulus on a 0-100 numerical rating scale (NRS), ranging from 0, denoting "no pain", to 100, denoting "the worst imaginable pain". Seven predetermined temperatures (44, 45, 46, 47, 48, 49 or 50°C) are presented 7 times in a random block-ordered design (total of 49 stimuli) (Treister, Eaton, Trudeau, Elder, & P Katz, 2017). Knowing both the intensity of the stimuli and the pain score reported in response to each stimulus allows the assessment of how accurate, consistent and reliable each subject is in reporting pain. FAST has three main outcomes. R2, coefficient of determination, informs about the disparity between the predicted function and actual scores of the subjects and it's a measure of accuracy or reliability. R2 is calculated by using a power model regression. Close concordance between actual and predicted scores are expressed by higher R2 indicating higher accuracy and reliability. ICC, intraclass correlation, is a measure of reliability. It is computed using a 2-way mixed model for the 7 presentations of each of the 7 stimuli intensities. Higher values of ICC indicate a high agreement in responses to the same stimuli over several presentations, thus a high degree of reliability. CoV, coefficient of variation is the ratio of the standard deviation to the mean, calculated separately for each stimulus intensity. A higher CoV demonstrates a larger variability in reporting.

FAST is well tolerated, it is not influenced by habituation, and has been found to have good reliability (Treister et al., 2017). A recent study utilizing the FAST has shown that pain reporting skills varied between subjects and that the FAST results correlated with changes in clinical pain. This study enrolled subjects with

chronic osteoarthritis (OA) who performed FAST followed by an exercise task (e.g. climbing staircases), expected to increase levels of pain. The patients rated their clinical pain before and after the stairs climbing. It was found that the FAST ICC significantly predicted the change in the subject's clinical pain. Exercise is expected to increase OA pain, and accurate pain reporters are expected to demonstrate the expected change in pain. The positive correlation between the FAST ICC and the change in clinical pain following exercise implies that those who demonstrated greater pain reporting skills (higher ICC) reported greater increases in their clinical pain following exercise. The result suggests that by using FAST one can identify subjects who can more accurately report changes in clinical pain. A second study enrolled patients with painful diabetic neuropathy (PDN) (Treister et al., 2018). This study aimed to assess if pain reporting accuracy could be improved by an evoked-pain training, using the Accurate Pain Reporting Training (APRT), a program developed by the same laboratory, based on multiple applications of FAST, while providing feedback on pain reporting accuracy between each FAST application. Patients were first randomly included into Training and No-Training interventions and subsequently, were randomized into a double-blind crossover trial of Pregabalin (PGN). According to previous studies (Harris et al., 2005; Farrar et al., 2014) and Treister et al 2017, here again the variability in pain reporting was related to the response in placebo conditions. Interestingly, here it was found that the training program improved the accuracy outcome (R2) and also reduced the placebo response.

It is unclear why increasing symptom reporting accuracy would impact the placebo response. Psychological expectations due to instructions, conditioning, and social learning might be the reason. Previous research also suggested that patients inconsistent in reporting their pain show constant inconsistency over time and individuals with large pain fluctuations are more likely to respond to placebo or respond well to both the analgesic and placebo (Harris et al., 2005). A recent study aimed to increase our understanding of the shared underling mechanisms. Healthy subjects underwent FAST and placebo response (assessed using tonic heat pain stimuli with 44°, 46.5° and 48°) with stimuli evoking mild, moderate and severe pain. These heat stimuli were given before subjects received a sugar pill and once again, after they took the sugar pill. The results highlight a negative

correlation between R2 FAST outcome measure and the placebo effect for severe pain, which means that greater accuracy and reliability was associated with less placebo effect. Similar, but non-significant results were found for mild and moderate pain (Honigman, Asaad &Treister, 2018). The hypothesis proposed for these results is that the more focused and accurately individuals can perceive bodily signals, more accurate and with less variability the FAST outcomes will be, and less affected by external cues, suggestions or expectations, which derive the placebo response.

However, further studies are needed to fully understand why some individuals are more accurate in their pain reports while other are less. It is also unknown if being accurate is a general trait, such that other sensations are reported accurately, or is it a pain specific trait, that is not related to the ability to accurately report other sensations.

1.3 Interoception

In contrast to exteroception, the processing of input from outside the body (vision, hearing, smell, taste and touch, with touch and taste having components of both), interoception is the sensitivity towards the physiological condition of one's body. It is crucial to the generation and perception of bodily sensations such as pain, temperature, hunger, thirst, vasomotor flush and respiration. Thus, interoception is a multimodal construct that includes several physiological channels that integrates multisensorial signals processed by internal viscera, baroreceptors, chemosensors, and surface temperature receptors and nociceptors. All these signals influence subjective perception of the body state and contribute to subjective feelings and the sense of self (Craig, 2003, 2009; Ceunen et al., 2016). The concept of interoception, previously seen as the sense of visceral sensations, is currently defined as "the sense of the physiological condition of the entire body". This definition highlights the crucial role of interoception which allows the organism to regulate itself through feedback processes (Craig 2002, 2015; Critchley & Harrison, 2013).

Previous research on Interoception highlights the role of vagus nerve and of the small-diameter fibres (Aδ and C) that converge in spinal dorsal horn lamina I. Both are implicated in the spinothalamocortical pathway (figure 1), the pathway

that conveys information regarding pain, visceral and cardiorespiratory inputs that later activate insular cortex (Strigo & Craig, 2016; Cameron, 2001; Craig, 2002, 2003; Critchley & Harrison, 2013; Critchley, Wiens, Rotshtein, Öhman & Dolan, 2004). Neurons in the spinal lamina I project into the nucleus of the solitary tract (NTS), parabrachial nucleus, periaqueductal gray, and other brainstem autonomic nuclei. Then, in the posterior and basal ventromedial nucleus of the thalamus, arises the main relay of viscerosensory and gustatory information within the spinothalamic tract, projecting onto hypothalamus, amygdala, orbitofrontal cortex, anterior cingulate cortex (ACC), and insular cortex (Craig, 2002, 2003; Strigo & Craig, 2016; Avery 2015, 2017).

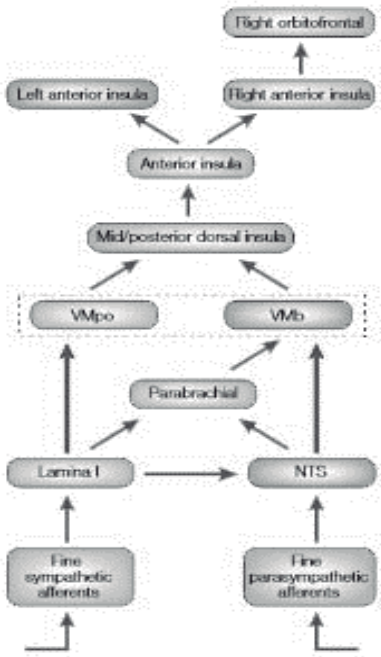

Figure 2 Organizational chart for interoception; nucleus of the solitary tract (NTS); ventromedial thalamic nucleus (VMb); ventromedial nucleus (VMpo) (Craig, 2002).

Accordingly, the information processed by the posterior insula is integrated in the mid-insula which also receives inputs from secondary somatosensory cortex (thus allowing integration of non-homeostatic information) (Kuehn, Mueller, Lohmann & Schuetz-Bosbach, 2015). Mid-insula is considered the locus of cross-modality integration, with efferents to the amygdala (stimulus salience

and emotional memories) and hypothalamus (state of the autonomic nervous system and of ongoing metabolic processes) (figure 2) (Ceunen, VlaeyenJ & Van Diest, 2016).

Lastly, anterior insular cortex is essential for the conscious interoception reflecting the reciprocal connections with higher order structures like anterior cingulate cortex, ventromedial prefrontal cortex and dorsolateral prefrontal cortex. Somatosensorial and somatomotor cortex also play important roles in this system, and are preferentially activated by aversive stimuli (Craig, 2002; 2003; 2009; Zu Eulenburg, Baumgärtner, Treede & Dieterich,2013). Studies also highlight the importance of the connections between anterior insular cortex, more specifically the right anterior insula (which integrates the sensation and the interoceptive system) and the close relation with ACC (which is responsible for motivational behaviour that participates in emotion) leading to emotional behaviour awareness (Pollatos et al., 2005; Critchley et al., 2004; Kuehn, Mueller, Lohmann & Schuetz-Bosbach, 2015).

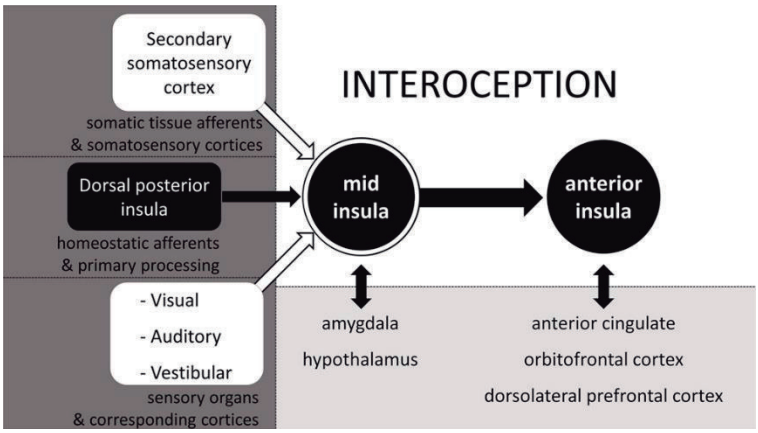

Figure 3. Integration of activity in progression from the posterior insula (left) through the mid-insula to the anterior insula (right). (Ceunen, VlaeyenJ & Van Diest, 2016)

The research interest on interoception has grown exponentially over the past 10 years. In one of the first and most influential peripheral theories, the James–Lange theory of emotion, it was suggested that signals generated from the body, such as the sensation of the heartbeat and respiration, are fundamental for the subjective experience of emotion. In this theory, an emotive stimulus automatically initiates visceral, vascular and somatic responses. Other theories,

specifically bodily feedback theories, proposed that the emotion experience is a product of cognitive-affective appraisal of bodily arousal (e.g. somatic markers by Damasio, 2000). These theories state that the identification of the changes in the generation and perception of bodily responses, are crucial for the variability in emotion experience. This was found both in central and peripheral processing of emotional stimuli (Craig 2002, 2015; Pollatos et al., 2005, 2007; 2012; Herbert et al., 2007), as well as cognitive processes like intuition and decision (Dunn et al., 2010). In other words, these evidences suggest that the more accurate in perceiving bodily activity the individual is, the stronger the relationship between such bodily changes and emotional experience and cognitive processing.

Despite theoretical suggestions of multiple integrations of the interoceptive information it is still unknown whether there is a general interoceptive ability. To clarify the field, several authors have proposed different models and tried to detail interoception theoretical construct (for a review see Di Lernia, Serino & Riva, 2016). One of the most influential is the theoretical model proposed by Garfinkel Seth, Barrett, Suzuki & Critchley (2015). In their model, they suggest that interoception can be divided into three different concepts: interoceptive accuracy (IAc), interoceptive sensibility (IS), and interoceptive awareness (IAw) (Garfinkel et al., 2015). “Interoceptive accuracy” is the objective ability in perceiving internal (bodily) signals and sensations, investigated for example, by means of heartbeat procedures related to cardiovascular perception (Garfinkel et al., 2015; Calì, Ambrosini, Picconi, Mehling & Committeri, 2015). These measures are sensitive to relevant individual differences (e.g., Critchley et al., 2004; Pollatos, 2012; Dunn et al., 2010) and to affective dimensions such as intensity (e.g., Wiens, Mezzacappa, & Katkin, 2000; Pollatos et al., 2012).

One of the most frequently used method to asses interoception is the heartbeat tracking method developed by Schandry (Schandry, 1981; Kleckner, Wormwood, Simmons, Barrett & Quigley, 2015). In this method, participants are fitted to an ECG, which records their true heartbeat through the entire task. Thereafter, subjects are asked to silently count their own heartbeats through three or four intervals with varying duration ranging from 25-55 seconds and to report the number of heartbeats counted for each interval. Individuals are asked to avoid touching their body or use any kind of physical manipulation to directly

feel their heartbeats. The outcome result is calculated by comparing the number of actual and reported heartbeats (Schandry, 1981). Studies using this task exhibited association between heartbeat tracking accuracy and memory for emotional words and decision making in complex situations (Werner, Peres, Duschek, & Schandry, 2009; Werner, Jung, Duschek & Schandry, 2009). Moreover, heartbeat tracking accuracy was also linked to subjective arousal while rating emotional images, and increasing IA promoted intuitive decision making in advantageous or disadvantageous choices dependent on the anticipatory bodily signals (Dunn et al., 2010). This method elicits activation of neuroanatomical structures such as thalamus, insula, medial frontal/dorsal cingulate, inferior frontal gyrus, as well as the somatomotor cortex (Pollatos, Schandry, Auer & Kaufman, 2007).

This method is widely used and relatively easy to perform in a research setting, with relatively short task duration (10–15 min). However, it has also some limitation, particularly related to the impact of expectations on the performance (e.g., knowledge of one's typical heart rate) (for revision of procedures see Kleckner, Wormwood, Simmons, Barrett & Quigley, 2015).

Although the most commonly used task is the heartbeat mental tracking, other methods to assess this modality were developed. Heartbeat discrimination task, also known as the modified Whitehead task (Whitehead, Drescher, Heiman, & Blackwell, 1977), is another example. In this task, participants are fitted to an ECG to acquire the true heartbeat. A series of 10 exteroceptive tones or visual inputs triggered by the R-spike in ECG are presented to either coincide or not coincide with the perception of those heartbeats. The subject's task is to discriminate whether the tones series presented are coincident (tones are presented 200 ms after each R-spike) or not coincident (tones presented 500 ms after each R-spike) with his heartbeat (Whitehead, Drescher, Heiman & Blackwell, 1977; Schulz et al., 2013). Studies using this method found that better IA detectors had greater experience of emotion while watching video clips with emotional valence (Wiens et al., 2000). This task has the advantageous of not being influenced by expectations, but it also implies different cognitive resources when compared to Schandry task. The later requires attention to visceral

sensations, while the Whitehead tasks require a focus on visceral sensations and exteroceptive stimuli concurrently.

Interoceptive Sensibility (IS), another concept proposed in the Garfinkel et al model, is considered as a subjective, self-evaluated characterological trait, assessed by questionnaires. Its frequently assessed using questionnaires that assess the extent to which individuals are able to perceive their internal sensations (e.g Multidimensional Assessment of Interoceptive Awareness, MAIA, Mehling et al., 2012; Interoception Sensory Questionnaire, by Fiene, Ireland & Brownlow, 2018; Body Awareness Questionnaire, see Shields, Mallory & Simon, 1989; Big Five Inventory see Benet-Martínez & John, 1998; John, Donahue, & Kentle, 1991; Five Factor Mindfulness Questionnaire, Baer et al., 2008; Self Awareness Questionnaire, Longarzo et al., 2015).

One of the most studied questionnaires in this research field is MAIA. It was developed by Mehling and colleagues (2012) and aimed to evaluate interoception as a multidimensional concept. MAIA has been developed based on the theoretical rational that several factors contribute to this construct like attentional styles, emotional awareness, anticipation and past experiences, abstraction and confidence of information arising within the body sensation. This may have therapeutic implications for clinical conditions, like anxiety, or helping to understand which aspects of body awareness are related to clinical outcomes, thus directing the therapies toward them.

The original version of MAIA is composed of 32 items. This has 8 different sub-scales to evaluate several component of interoception sensitivity: (1) Noticing, the awareness of one's body sensations; (2) Not-distracting, the tendency not to ignore or distract oneself from sensations of pain or discomfort; (3) Not-worrying, the tendency not to experience emotional distress or worry with sensations of pain or discomfort; (4) Attention regulation, the ability to sustain and control attention to body sensation; (5) Emotional awareness, the awareness of the connection between body sensations and emotional states; (6) Self-regulation, the ability to regulate psychological distress by attention to body sensations; (7) Body-listening: the tendency to use the insight abilities while listening the body and (8) Trusting: the experience of one's body as safe and trustworthy. The results indicated good psychometric properties, supporting the

construct validity and internal consistency reliability of the MAIA scales. Accordingly, association were found between MAIA scales and scales of related constructs (among others, Five Factor Mindfulness Questionnaire (Baer et al., 2008), Body Consciousness Questionnaire (Miller, Murphy & Bush, 1981), Pain Catastrophizing Scale (Sullivan, Bishop & Pivik, 1995), State-Trait Anxiety Inventory (Spielberger, 1983), Difficults in Emotion Regulation Scale (Gratz & Roemer, 2004). Recently, MAIA was translated and validated into a Portuguese by Machorrinho (2017). The Portuguese version is composed of 33 items scored on a 6-points Likert scale. This multidimensional instrument measures IAw on seven scales: (1) Noticing (3 items); (2) Not-distracting, (4 items); (3) Not-worrying, (4 items); (4) Attention regulation, (7 items); (5) Emotional awareness, (5 items); (6) Self-regulation, (7 items); (7) Trusting, (3 items). The score is calculated for each scale by averaging the scores of individual items, and thus can range 0–5. Higher values in the questionnaire reveal higher IS (Machorrinho, 2017; Mehling et al., 2012).

Interoceptive awareness (IAw), is the metacognitive awareness of interoceptive accuracy (Garfinkel, et al., 2015). This measure is usually assessed immediately after the end of the heartbeat detection task. The subject is asked to rate his confidence in his perceived accuracy response, (e.g. using a paper and pencil marking his response on a continuous visual analogue scale from “No heartbeat awareness” to “Full perception of heartbeat” (Garfinkel et al., 2015). These confidence measures highlight the relationship between subjective (perceived) and objective (actual) interoceptive ability (Khalsa et al., 2008). From another viewpoint, it is also possible to quantify explicitly how the confidence predicts accuracy within a given individual using more sophisticated analytic approaches (e.g. receiver operating characteristic (ROC) curves or trial-by-trial confidence – accuracy correlations) (Green & Sweets, 1966; Garfinkel et al., 2015).

Garfinkel and colleagues (2013, 2015) proposed an hierarquical model of interoception, with IS as the base, revealing a tendency/trait to be internally focused to body sensations, with influences on IA performance and IAw (Calì, Ambrosini, Picconi, Mehling & Committeri, 2015). Previous research has already found that IS and IA do not predict each other or have significant correlations

(Mcfarland, 1975; Whitehead, et al., 1977). In a recent research, Garfinkel and colleagues (2015) found that the three dimensions were distinct and dissociable, but within the group of subjects with better IA scores, IA was predicted by IAw and IS, revealing a possible central effect of this construct, supporting the remain. IAw and IS also seems to be independent (i.e. not predicted by each other).

Further evidence for this model came from studies with experienced meditators and non-practices of contemplative therapies, showing that meditators don't differ in IA but rate their performance as better. This means that meditation increase measures of confidence, which increase measures in awareness, when match IAc with better performance in IAw. (Khalsa et al., 2008). Fischer, Messner & Pollatos, 2017 also measured the behaviour of these three dimensions of interoception towards an implementation of a 8-week mindfulness-based stress approach, to increase attention to bodily sensations, called body scan (Parkin et al., 2014). The results showed that participants were able to detect their heartbeat more accurately after the training approach, supporting the idea that paying attention to the body in a mindful way has a beneficial impact on interoception (Parkin et al., 2014) and also on the confidence in the interoception. However, no change in IS was observed. This might have happened because of methodological reasons: the measure used to assess IS was the Eating Disorder Inventory (Garner, Olmstead & Polivy, 1983) which was not a questionnaire directed to general body awareness, as MAIA is.

In summary, even though some contemplative practices like meditation and biofeedback are assumed to improve the sensation of bodily signals and attention towards own body, other studies suggest no such affect concerning heartbeat perception performance (Nielsen and Kaszniak, 2006; Khalsa et al., 2008). However, several studies, including mindfulness, only improved the measures of interoceptive confidence, functionality and quality of life, distinguishing individuals more experience in this practice as more confident in interoception tasks than the non-meditators (Khalsa et al., 2008; Parkin et al., 2013; Mehling, 2016; Farb et al.,2015; Mehling, 2016).

The increase interest in the ability to increase the interoception reporting skills described in these studies is due to its close and crucial link known to exist between interoception and other relevant human neurocognitive processes, such

as memories, decision making, perception of time, emotion experience, health and pain (Ceunen, Vlaeyen, & Van Diest, 2016; Schandry et al., 1981; Wiens, 2005; Craig, 2009b; Pollatos and Schandry, 2007; Garfinkel et al., 2014).

1.4 Interoception and other sensory modalities

The relation between different interoception modalities has been intriguing. The studies conducted under this topic have not found clear-cut results and the relations are still not easy to understand. One of the reasons is that different studies assess different modalities and use diverse methods to assess the same modality. Several interoceptive modalities have been measured in this field, such as gastric function, assessed by invasive, (Whitehead & Drescher, 1981), and more recently, non-invasive methods like Water Load Test, to induce gastric distension and gastric neuromuscular activity, by ingesting room temperature, non-carbonated water (Chen, Lin, Chen & Huang, 2005; Herbert, Muth, Pollatos & Herbert, 2012). Regarding the gastrointestinal modality tasks of rectal and anal distensions are also used (Hobday et al., 2001). Another modality that is frequently included in interoception research is respiratory function (Daubenmier, Sze, Kerr, Kemeny & Mehling, 2013; Faull, Cox & Pattinson, 2016; Harver, Katkin & Bloch, 1993) using respiratory load task and respiratory discrimination (Zechman, Hall, & Hull, 1957; Webster & Colrain, 2000). In these tasks' participants must detect when a (or several) resistances have been introduced into a tube, through which they are breathing (Davenport, Chan, Zhang, Chou, 2007; Zhao, Martin, & Davenport, 2002). Tactile acuity task (Van Boven & Johnson, 1994) assess sensitivity for touch. It can be made using a series of grooved shaped pieces of plastic applied with bars and grooves aligned in one of two orthogonal directions. The participant is asked to identify which was the orientation of the stimulus. (Zu Eulenberg, Baumgärtner, Treede & Dieterich, 2013). In taste tasks, sweet, bitterness and the neutral flavours are sprayed into the oral cavity of the subject (e.g. Avery et al., 2015; Ferentzi et al., 2017) and he is asked to rate the perceived intensity and pleasantness of the stimulus.

The contemporary approach to interoception includes also the assessment of the lemniscal pathway, responsible for proprioception, the conscious perception

of joint angles and muscle tensions, of movement, posture, and balance (Craig, 2015; Goble, 2010) (see protocol in Ferentzi et al., 2018). Examples of tasks measuring this are the joint position matching, whereby individuals must replicate a reference joint angle in the absence of vision (ie, using proprioceptive information).

Based on the comparison of these modalities, two studies found moderate associations between heartbeat perception task and gastric perception (Whitehead and Drescher, 1980; Herbert et al., 2012) and another between the heartbeat task and the perception of skin conductance (Steptoe e Noll, 1997). Several other studies assessing perception of multiple interoception modalities, as detection of heartbeat, gastric and respiratory perception, did not found correlations between different modalities (Vaitl, 1996; Harver et al, 1993; Werner et al., 2009; Garfinkel et al 2016). A recent study investigated four interoceptive channels, namely heartbeat perception, pain threshold and pain tolerance, bitterness sensitivity and balancing ability (Ferentzi et al., 2017). They found no relations between these modalities. One interesting study, in chronic pain patients related two modalities, respiration and pain have found that healthy subjects who underwent a slow breathing approach reduced ratings of pain intensity and unpleasantness, while in fibromyalgia patients these relations were less reliable (Zautra, Fasman, Davis, Arthur & Craig, 2009).

A recently published study directly investigated the relations between a higher number of interoception modalities (Ferentzi et al., 2018). A multichannel approach was used, and six sensory channels were assessed: heartbeat, gastric, pain and bitter perception, proprioception and balancing ability. Correlations and factor analyses were performed, and the results indicated that there were no correlations or a common factor between different modalities. This suggest that the ability to perceive multiple dimensions from the same modality is integrated for a general perception of a specific sensory channel, but the same is not true between modalities. The current study aimed to investigate the relations between pain reporting accuracy and the ability to report other interoception modalities, such as taste and heartbeat.

1.5 Theoretical proposals

From a theoretical point of view, the absence of relations between different modalities is not clearly hypothesized. According to Craig's perspective (Craig, 2002, 2009; 2015) and other "embodied theories of emotion" (e.g.; Critchley, 2005; Damasio et al., 2000; Rainville et al., 2006) the information provided by sensory systems is essential for emotional processing and appraisals, and usually all contribute to a general interoception perception. More recently, Smith and Lane (2015) detailed this "general" interoception ability suggesting that emotional processing depend on three systems with hierarchical organization, from those that require lower cognitive appraisals to those that need higher cognitive appraisals. The first stage, called "generative", information convey by each sensory system is processed at somatosensory cortex and posterior insula. Only in the next stage of processing, the "perceptual", a "whole-body pattern" is created in the anterior insula, based on the integration of these discrete systems. Finally, in the third stage the anterior cingulate cortex, the emotional concepts are created using information from the lower level processing with "regulatory" higher systems. Between these systems, several feedback and feedforward processes modulate the appraisals, and may be related to other brain areas. Based on this model it may be hypothesized that each sensory modality is independently processed before integration to generate a more general "whole-body" assessment. It might be that the IA (Garfinkel et al., 2015) assessed for example using MAIA, as well as other psychological constructs may be processed at higher level than modality specific tasks. Accordingly, due to such differences in the design of studies comparing different interoception modalities, it is still unclear if there are relations between these modalities.

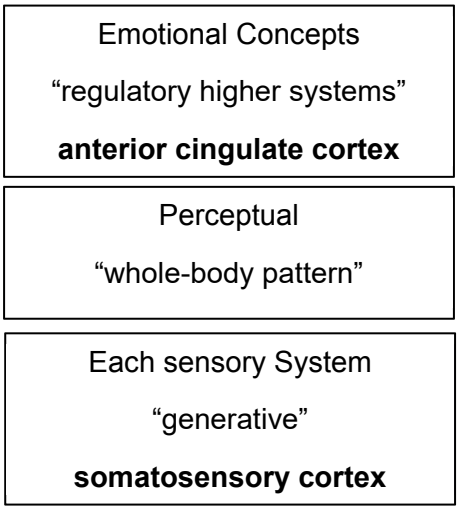

Figure 4. Model proposed by Smith and Lane (2015) on three hierarchical systems.

2. Submitted Manuscript

2.1 Introduction

Pain intensity, as intensities of other subjective experiences is challenging to measure. Both clinical and research findings depend on such subjective self-report assessments, which are reported on scales that are variably understood by subjects. These limitations are reflected in experts concerns regarding the appropriateness of pain intensity measures as primary outcomes in chronic pain populations (Ballantine & Sullivan, 2015), and in lack of use of such scales by pain clinicians (Bačkonja & Farrar, 2015).

Recent findings suggest that pain reporting accuracy vary across patients (Treister, Eaton, Trudeau, Elder & Katz, 2017), a characteristic that can be assessed by the Focused Analgesia Selection Test (FAST) task. The FAST is based on exposing subjects to repeated noxious stimuli of various intensities in blinded manner. Assessing the relations between the stimulus intensities and pain reports allow to assess the error variance component of one's pain intensity reports, or in other words, to quantify subject's ability to accurately report pain. As shown, subjects ability to accurately report pain in the FAST procedure relates to their ability to accurately report changes in clinical pain (Treister, Eaton, Trudeau, Elder & Katz, 2017).

The notion that the ability to accurately report pain can be assessed by an experimental procedure is novel; however, the assessment of reporting accuracy of other bodily sensations, termed interoception, has been intensively investigated. Previously seen merely as the sense of visceral sensations, interoception is currently defined as “the sense of the physiological condition of the entire body” (Ceunen, Vlaeyen, & Van Diest, 2016; Craig, 2015), often linked to pain and temperature, cardiorespiratory function, hunger, thirst, stress, vasomotor flush and respiration. Interoception has been assessed by several methods, based on various modalities. A common method is based on sensitivity to detect one's own heartbeats, termed the heartbeat detection task (Schandry, 1981). Other methods and questionnaires have been used to assess interoception (Flor, Fürst & Birbaumer, 1999; Garfinkel et al., 2016; Garfinkel,

Seth, Barrett, Suzuki, & Critchley, 2015; Harver, Katkin, & Bloch, 1993; Herbert, Muth, Pollatos, & Herbert, 2012; Mehling et al., 2012; Michael, Naveteur, Dupuy & Jacquot, 2015; Whitehead, Drescher, Heiman, & Blackwell, 1977).

Interoceptive signals ascend from the periphery in two main pathways (Craig, 2009), the spinothalamical and lemniscal tracts, which are integrated at multiple levels, among which the medial and the anterior insular cortex play a primary role (Engström, Karlsson, Landtblom & Craig, 2015). Given that interoceptive information, regardless of its origin, is processed by same brain structures, it is reasonable to assume that being able to accurately report pain would correlate with ability to accurately report other bodily sensations, which is, the aim of the current investigation. Specifically, possible relationships between pain-reporting accuracy and the ability to accurately detect heartbeat and tastes will be assessed.

2.2 Materials and Methods

Subjects:

The study sample included healthy volunteers, which were recruited from local Universities of Lisbon. Experiments were conducted in accordance with the Declaration of Helsinki and with the approval of the local Ethical Board. Written informed consent was obtained from each participant before the beginning of the experiment, and afterwards a code number was attributed to each subject. Participants were enrolled onto the study after meeting the following criteria: (1) age above 18; (2) absence of acute or chronic pain disorders; (3) no reports of psychiatric, cognitive, and /or neurological disorders; and (4) no chronic use of medications except for oral contraceptives. Participants were excluded if: (1) were pregnant or breastfeeding; (2) had any persistent or severe infection within 30 days of baseline; (3) had formal diagnosis of any uncontrolled medical condition and (4) were unable to provide informed consent, communicate and understand the purpose and the instructions of the study.

Instruments and procedures:

The Focused Analgesia Selection Test (FAST)

FAST was developed to assess pain-reporting skills in response to repeated administration of thermal noxious stimuli of varying intensities applied to ventral surface of the subject's non-dominant arm. It uses the Medoc® Thermal Sensory Analyzer II incorporating a Peltier element-based thermode (30 x 30 mm^2). Subjects were instructed to rate their perceived pain intensity in response to each stimulus on a 0-100 numerical rating scale (NRS), ranging from 0, denoting "no pain", to 100, denoting "the worst imaginable pain". The temperature was raised from a baseline of 32°C, peaked for 3 seconds at one out of 7 predetermined temperatures (44, 45, 46, 47, 48, 49 or 50°C) and then decreased down to baseline, with total stimulus duration (including ramping up and down) of 8 seconds. Each temperature was presented 7 times in a random block-ordered design (total of 49 stimuli), based on a previously described protocol (Treister, Eaton, Trudeau, Elder & Katz, 2017). The location of the thermode was adjusted every 10 stimuli to minimize sensitization and/or habituation effects with inter-

stimulus intervals (ISI) of 15 seconds. The FAST procedure duration is about 25 minutes.

Pain scores captured during the FAST were used to calculate the 3 FAST outcomes as follows: 1) R^2 was calculated by using a power model regression. Disparity between the predicted function and actual scores could be a result of inaccuracy or unreliability. Close concordance between actual and predicted scores are expressed by higher R^2, and suggests greater accuracy and reliability; 2) ICC was computed using a 2-way mixed model for the 7 presentations of each of the 7 stimuli intensities. An ICC score approaching 1 denotes a high degree of reliability (or the agreement in responses to the same stimulus over several presentations); 3) The CoV is the ratio of the SD to the mean, calculated separately for each stimulus intensity. The average CoV was calculated as the mean of 7 CoVs. A higher CoV demonstrates a larger variability in reporting.

Taste Perception task

This task is a modification of Hendi and Leshen (2014) procedure, which was developed to assess the sensitivity to salty and sweet taste. Unlike the original purpose, the procedure was modified to assess reporting accuracy of tastes, rather than sensitivity to tastes. The participants were asked to avoid eating, drinking (except water) and smoke 2 hours before the test. During the task subjects were requested to grade the intensity of five different concentrations of each flavor, administered on the tongue via oral sprays. Preparation of the sprays was as follows: for the most concentrated salty solution (vial 5), 37.45 g of NaCl was added to 250 cc (quarter-litter) of mineral water. For the second solution (vial 4), the first concentration was diluted by 1.5. For the third concentration (vial 3), the first solution was diluted by ratio of 1:3. The last two concentrations were diluted from the third (vial 2) and the forth (vial 1) concentrations, by 1:3. Preparation of the sugar solution was as follows: The highest concentration (vial 5) was of 67.5 grams of sugar in 250 cc (quarter-litter) of mineral water. The rest of the sprays were prepared by repeated dilution at a ratio of 1:2, except the second concentration (vial 4), that was prepared from the high concentration and diluted in ratio of 1:1. Mineral water with a maximum of 9mg of NaCl /L was used for both the salty and sugar solutions. The exact ratio of concentrations was determined based on pilot studies, aimed to identify concentrations that will be

perceived, on average, as distinct from each other. During the task, the experimenter sprayed each taste solution onto the participant's oral cavity in a semi-randomised order (excluding sequential concentrations). Between every two sprays subjects were requested to wash their oral cavity with fresh water. Subjects randomly began the taste task with either salty or sweet taste series, followed by the other taste. ISI between two consecutive administrations of sprays was about 10 seconds. Each concentration was repeated 5 times (a total of 25 repeats for each taste). The participants were asked to indicate how strong was the flavor, for each concentration of taste, on a NRS ranging from 0 "not feeling", to 100 "most strong". As in the FAST procedure, the taste procedure outcomes are the R^2, ICC and CoV, calculated in the same manner as in the FAST.

Heartbeat perception task

The heart beat perception task assesses the individuals' ability to be accurate in the perception of its heartbeat. This task, named the Mental Tracking Method, was developed by Schandry in 1981 in order to assess interoception accuracy using three heart beat counting phases with varying length (Schandry, 1981). First, participants fitted to physiological recording equipment to assess true heartbeat through electrocardiography (BITalino device, Plux Wireless Biosignals, SA, Lisbon, Portugal). The experimental task consisted of five minutes resting period to assess baseline measures. Then, when a voice signal was presented by a research assistant, the subject is asked to pay attention and count his/her heartbeats silently, focusing only on bodily feelings. Next, after offset voice signal was given, the subject is asked to report the number of counted heartbeats. The following instructions are given: "Without manually checking, count silently each heartbeat you feel in your body from the time you hear "start" to when you hear "stop". Subjects were instructed to avoid any kind of physical manipulation (pressure points, respiratory manipulation) that might ease detection. The task was performed three times with varying in length (25, 35, 45 seconds) in the following order: rest (60s) - perception (25s) – rest (30s) – perception (35s) – rest (30s) – perception (45s) – rest (60s). The subject was unaware to the different length of each round. Heart rate and respiration were assessed using Ag/AgCl electrodes per Eithovens' triangle and respiratory belts,

respectively, connected to the BITalino device. Heartbeat perception accuracy was calculated, for each subject, as an error score between counted heartbeats reported and actual heartbeats obtained by ECG, according to the formula:

$$\text{IAc score} = \frac{1}{3}\sum[1-(recordedheartbeats - countedheartbeats)/recordedheartbeats]$$

IA vary between 0 - 1. Higher scores indicate better IAc.

Questionnaires

Sociodemographic Questionnaire:

Participants indicated their age, sex, height and weight, health condition, medication (last 48 hours, contraceptives), last menstruation and consumption habits (alcohol, tobacco, drugs).

In addition, the following patients reported outcome measures, which are known for being related to pain or interoception were assessed:

Perceived Stress Scale (PSS):

Perceived Stress Scale is a brief instrument, used in community samples to assess to what degree, situations in participants' life were appraised as stressful (Cohen, Kamarck & Mermelstein, 1983). In response to each item, participants report their feelings on a five-likert scale during last month. The validated Portuguese version of this instrument was considered adequate and was used (Moreira, 2002).

Hospital Anxiety and Depression Scale (HADS):

The Hospital Depression and Anxiety Scale is a brief instrument commonly used to assess anxiety and depression in non-psychiatric population (Zigmond & Snaith, 1983). It consists of 14 items (response scale 0–3), which are divided into 2 subscales measuring either anxiety or depression feelings during past week. The validated Portuguese version was used (McIntyre, Pereira, Soares, Gouveia & Silva, 1999). The results vary from 0 to 21, with higher scores indicating higher levels of depression or anxiety. The severity of anxiety and depression is classified as: values 0-7 = normal, 8-10 = light, 11-14 = mild and 15-21 = severe.

Multidimensional Assessment of Interoceptive Awareness (MAIA):

Interoceptive awareness (IAw) was assessed by the Portuguese version (Machorrinho, 2017) of the original English-language MAIA (Mehling et al., 2012). The MAIA is composed of 33 items scored on a 6-points Likert scale. This multidimensional instrument measures IAw on seven scales: (1) Noticing, the awareness of one's body sensations (3 items); (2) Not-distracting, the tendency not to ignore or distract oneself from sensations of pain or discomfort (4 items); (3) Not-worrying, the tendency not to experience emotional distress or worry with sensations of pain or discomfort (4 items); (4) Attention regulation, the ability to sustain and control attention to body sensation (7 items); (5) Emotional awareness, the awareness of the connection between body sensations and emotional states (5 items); (6) Self-regulation, the ability to regulate psychological distress by attention to body sensations (7 items); (7) Trusting: the experience of one's body as safe and trustworthy (3 items). The score for each scale is calculated by averaging the scores of individual items, and thus can range 0–5.

Experimental protocol

Subjects were asked to refrain from: (1) taking any analgesics, beta blockers (that influences heart function) and any over-the-counter medications during the day of the study visit; (2) eating and drinking (besides water) 2h hours prior to the study session; and (3) smoking 2h hours prior to the study.

The experiments were conducted at NeuroSer Clinic and university laboratory. At the beginning of the experimental session, all subjects underwent short training in order to familiarize them with the devices, the sensations evoked by the painful stimulation, and the rating task. After the familiarization stage the experiment begun with the FAST procedure. Thereafter, all subjects preformed the heart beat task, which begun with 5 minutes baseline measures recordings, followed by a 10 sec familiarization phase. Upon completion of the heartbeat detection task, the taste procedure was familiarized and preformed. The total duration of the experimental session was approximately 1 and a half hours, and participants were rewarded for their participation with credits for neuroscience subject.

Statistical Analyses

Data were processed and analysed using Excel (Microsoft Corp, Redmond, WA, USA), and SPSS software version 23 (SPSS, Inc., Chicago, IL, USA).

Descriptive statistics were used to present demographic and baseline characteristics.

As most variables were non-normally distributed (tested by Kolmogorov–Smirnov and Shapiro–Wilk tests), data were analysed with nonparametric tests. Friedman's tests (followed by Wilcoxon post hoc test, when applicable) were used to assess differences in pain and taste (sugar and salt) scores. Spearman's correlations were used to assess relations between the accuracy tasks (FAST and taste) and interoception measures (heartbeat task and MAIA), as well associations with pain-related psychological questionnaires (PSS and HADS). In all figures, data presented as mean ± SD unless specified otherwise. Statistical significance was defined as $P \leq 0.05$.

2.3 Results

Participants' Characteristics

The study sample included 60 volunteers (29 men and 31 women), ranging in age from 18 to 53 with mean ± standard deviation (SD) of 23.63 ± 6.31 years. Table 1 depicts the socio-demographic data of the entire sample.

Table 1. Demographic data of the study population (n=60)

Characteristics	Mean ± Standard Deviation	Frequency (%)	Range
BMI (Kg/m)	22.7 ± 3.5	-	14.1-32.7
Education High school Undergraduate Graduate	-	 40 (66.7%) 18 (30%) 2 (3.3%	-
Marital Status Single Married	-	- 56(93.3%) 4(6.7%)	-

FAST outcome measures

Mean pain intensities reported in response to each of the seven stimuli intensities are presented in Figure 1. Group mean ± SD responses ranged from 19.65 ± 17.7 for the lowest stimulus intensity (44°C) to 62.59 ± 23.8 for the highest stimulus (50°C). Mean pain scores significantly differed from each other (Friedman's test, chi-square 288.83; P <.001). Post hoc Wilcoxon test revealed significant difference between all stimuli intensities (P<0.001) apart from a non-significant difference when comparing between 44°C and 45°C (P=0.216).

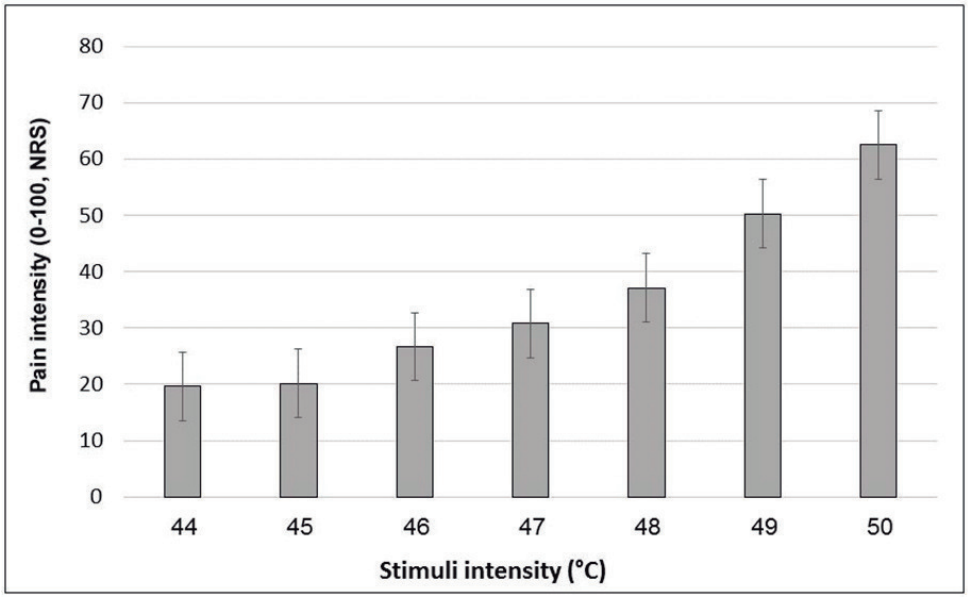

Figure 1. Mean pain scores in response to the 7 FAST stimuli by stimulus intensity.

Note: Black bars represent the average pain scores in response to the 7 stimuli at each intensity. Error bars represent the standard error of the mean.

Descriptive statistics of the FAST outcomes are described in Table 2. The R^2, ICC, and CoV indicated that subjects' pain reporting skills were widely distributed. R^2 had a mean of 0.45 (range 0.01–0.77), ICC with mean of 0.60 (range 0.08–0.87), whereas CoV had a mean of 0.58 (range 0.05–1.56).

Table 2. FAST outcomes

	R^2	ICC	CoV
Mean (SD)	0.453 (0.16)	0.602 (0.16)	0.577 (0.38)
Median	0.49	0.62	0.49
Minimum	0.01	0.08	0.05
Maximum	0.77	0.87	1.56

Note: FAST, focused analgesia selection test; SD, standard deviation; ICC, intraclass correlation coefficient; CoV, coefficient of variation

Interoception outcome measures

Interoception Task:

The mean heartbeat perception score was 0.65 (range 0.00–0.98), with median score of 0.69. This wide range of scores suggests that participants differ in their interoception accuracy, as assessed by the heartbeat detection task.

Taste task outcome measures:

Mean taste intensity ratings reported in response to each of the five concentrations for both sugar and salt are presented in Figure 2. Group mean ± SD responses ranged from 2.22 (± 3.53) and 1.95 (±3.01 SD) for the lowest stimuli intensity (Salt 1 and Sugar 1 respectively) up to 54.02 (± 25.19) and 33.73 (± 25.61) for the highest stimuli (Salt 5 and Sugar 5, respectively). Mean taste scores of salt significantly differed from each other (Friedman's test, chi-square 231.56, p<.001) as well as the mean taste scores of sugar (Friedman's test, chi-square 225.15, p<.001). Post hoc Wilcoxon test revealed significant difference between each concentration of both sugar and salt (*P*<0.001). Descriptive statistics of the tastes outcomes are described in Table 3. The R^2, ICC, and CoV indicated that subjects' taste reporting skills were widely distributed.

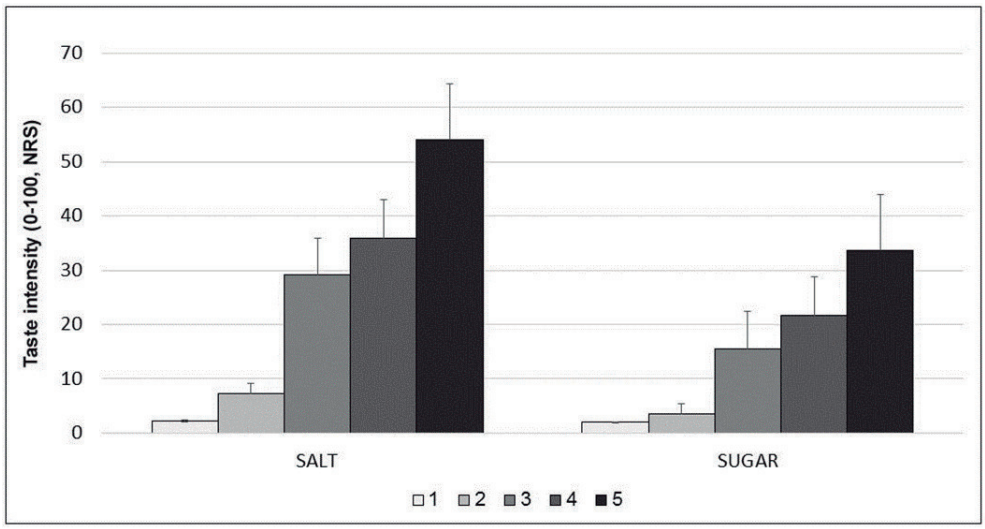

Figure 2. Mean intensity taste scores.

Note: Each bar represents the average taste scores in response to the different salt/sugar concentrations. Error bars represent the standard error of the mean. Taste concentrations are labeled 1 to 5, from lowest to highest concentration.

Table 3. Taste task outcomes

SALT	**R^2**	**ICC**	**CoV**
Mean (SD)	0.686 (0.14)	0.831 (0.12)	0.475 (0.21)
Median	0.72	0.86	0.44
Minimum	0.34	0.17	0.12
Maximum	0.92	0.96	0.93
SUGAR	**R^2**	**ICC**	**CoV**
Mean (SD)	0.614 (0.18)	0.774 (0.15)	0.496 (0.22)
Median	0.65	0.81	0.47
Minimum	0.03	0.06	0.09
Maximum	0.87	0.96	1.12

Note: SD, standard deviation; ICC, intraclass correlation coefficient; CoV, coefficient of variation.

Interoception as assessed by the MAIA questionnaire:

Table 4 depicts the results of the Multidimensional Assessment of Introceptive Awareness (MAIA) questionnaire.

Table 4. A summary of the values distribution of the MAIA questionnaire

MAIA sub-scales	Mean ± SD	Median	Min-Max
Noticing	3.38 ± 0.9	3.33	0-5
Not Distracting	1.66 ± 0.9	1.50	0-4.5
Not worrying	2.70 ± 1.1	3.0	0.25-5
Attention Regulation	3.02 ± 0.8	3.0	1.14-4.71
Emotional Awareness	3.64 ± 0.8	3.60	1.80-5
Self-Regulation	2.67 ± 0.9	2.57	1-4.43
Trusting	3.81 ± 0.8	4.0	1.67-5
TOTAL	5.44 ± 13.7	2.91	1.88-95

Cross-modal associations of accuracy reporting

Positive correlation was found between reporting accuracy of the two tastes. Subjects with high salt ICC had a high sugar ICC values (Spearman's r=0.477, *P*<0.001). No significant cross-modal correlations were found between any of the accuracy tasks (FAST, heartbeat task and taste) (*P*>0.05 for all outcome measures). No significant correlations were found between Interoception task and the MAIA questionnaire (P>0.05).

Relations between pain-related psychological questionnaires and measures of accuracy

Table 5 depicts the psychological characteristics. No significant correlations were found between any of the psychological measures and accuracy measures (FAST, heartbeat, and taste).

Table 5. A summary of the values distribution of the psychological questionnaire

Questionnaires	Mean ± Standard Deviation	Median
PSS	18.45 ± 7.15	18.0
HADS-*total*	11.03 ± 6.10	9.0
HADS-*anxiety*	7.03 ± 3.58	7.0
HADS-*depression*	3.95 ± 3.22	3.0

Note: PSS, perceived stress scale; HADS, hospital anxiety and depression scale.

2.4 Discussion

The aim of the current study was to investigate if the ability to accurately report pain is correlated with the ability to accuracy report other bodily sensations. Our hypothesis was rejected: No correlations were found between reporting accuracy of pain intensity and accuracy of reporting other sensations.

Our results suggest that interoceptive accuracy covary across different modalities. Several other studies assessing perception of multiple interoception modalities, as detection of heartbeat, gastric and respiratory perception, did not found correlations between accuracy of reporting different modalities (Garfinkel et al., 2016; Harver, Katkin & Bloch, 1993; Ferentzi et al., 2017; Vaitl, 1996; Werner, Duschek, Mattern & Schandry, 2009). As such, a recent study directly investigated the relations between six interoception modalities tasks, including heartbeat, gastric, pain, bitter perception, proprioception and balancing ability (Ferentzi, et al., 2018). The results indicated that there were no correlations or a common factor between different modalities. As in our case, the authors did find correlations within measures of the same sensory modality. This suggests that reporting accuracy is a characteristic that can be generalized within, but not between modalities. In contrast to our and Ferentzi et al., (2018) results, previous studies shown moderate associations between heartbeat perception task and gastric perception (Garfinkel et al., 2016; Whitehead & Drescher, 1980) and between the heartbeat task and the perception of skin conductance (Steptoe & Noll, 1997).

Methodological differences can account for these seemingly contrasting findings. Commonly, methods involved not only different sensory channels, but also different tasks modalities. For example, in Ferentzi et al (2018) pain was assessed using a threshold and tolerance tasks. These two measures assess pain perception and as such, correlations between such measures does not necessarily reflect pain-reporting accuracy. Some studies found correlations between heartbeat perception task and pain perception (Herbert, Pollatos & Schandry, 2007; Pollatos, Füstös Critchley, 2012; Wiens, Mezzacappa & Katkin, 2000) while other did not (Werner, Duschek, Mattern & Schandry, 2009). Unlike pain perception measures (eg pain thresholds and tolerance), the FAST outcomes capture different aspects of pain reporting accuracy, and are less

affected by pain sensitivity. Similarly, a single Visual Analogue Scale score of intensity (or unpleasantness) of a taste solution represent the sensitivity (or hedonic assessment) of subjects to a given taste, rather than subject's ability to accurately report intensity of tastes (Ferentzi et al., 2018).

Aligned with previous research findings, in our study, the interoception tasks were not significantly correlated with the measures assessed by the MAIA questionnaire, indicative that these tasks do not measure the same constructs. This observation is in line with the theoretical model proposed by Garfinkel and colleagues (2015) that suggests that “interoceptive sensibility”, the subjective self-evaluated trait assessed by questionnaires (e.g. MAIA) does not correlate with “interoception accuracy”, an objective measure (Garfinkel, Seth, Barrett, Suzuki, & Critchley, 2015; Calì, Ambrosini, Picconi, Mehling & Committeri,2015).

Our findings of lack of correlations between interoceptive modalities support the notion that the accuracy is specific for each sensory system and can’t be generalized across modalities or inferred from one modality to another. Craig's perspective, suggests that even though the interoception integrates several different sensations from the body running in the same neuronal pathways, interoception is a general homeostatic function (Craig, 2002; 2003; 2009; 2015). More recently, Smith and Lane (2015) proposed a specific organization for the specific sensory information and the general feelings of interoception. They considered that interoception is processed on three hierarchical systems: the “generative”, processing information from each sensory system (involving somatosensory cortex and posterior insula), the “perceptual”, where a first “whole-body pattern” is constructed (in the anterior insula) and the “regulatory”, the final stage (integrating the anterior cingulate cortex) where the emotional concepts are created using information from the lower level processing with higher systems (Smith & Lane, 2015). The lack of cross-modal correlations in reporting accuracy observed in our study is aligned with this above-mentioned model.

Treister et al. (2018) have recently showed that pain accuracy is a trainable skill that can be improved by an evoked-pain training approach. The lack of correlations between accuracy reporting of various modalities found in this study

suggest that improving reporting accuracy of one modality will probably not affect the accuracy reporting of other modalities.

In summary, the current study demonstrated lack of associations between pain reporting accuracy and the accuracy of reporting other sensations, suggesting that interoceptive accuracy cannot be generalized across modalities. Further investigation is needed in order to understand differences in the accuracy in symptom reporting and its clinical relevance.

Acknowledgments

We wish to thanks Neuroser (http://neuroser.pt/) and particularly Dra Ana Paula Pereira for providing the place in which data collection was performed.

Disclosure

The author reports no conflicts of interest in this work.

3. General Conclusion

The main finding of this study was that the accuracy in pain reporting is not related to the accuracy in reporting other bodily sensations. However, there are relations between the ability to be accurate within the same modality.

The relations between different interoception modalities have been studied before but using different paradigms for each modality: the previous studies compared the results not only between different stimulus modalities, but either between different measures. To the best of our knowledge this was the first time that two similar interoception tasks were developed: FAST and taste are the same task and allow the same outcome measures. Thus, the difference between the tasks in mainly the stimulus modality (pain and taste).

Accordingly, the results of the current study do support the notion that the ability to be accurate in reporting bodily signals is not a general trait but depends on the stimulus modality. Those who are more accurate in pain reporting are not more accurate in perceiving other body signals. This was found comparing stimulus modalities (taste and heartbeat) and even when comparing the pain reporting accuracy and the subject's perspective of their ability to perceive body signals, using the MAIA questionnaire, that assesses Interoception Awareness.

This study has limitations that should be overcome in the future. One is related to the recruitment and sample, which was a convenience sample, mostly from the Psychology course students. Using older and increase diversification of educational and other background variables could increase the generalization of the results.

Another limitation of the current study was the lack of a measure of pain sensitivity, a threshold or a tolerance task, that might also increase the knowledge regarding the pain sensitivity differences in the subjects with high and low accuracy. Even though the FAST does allow some assessment of pain sensitivity using the mean pain values of each temperature, a specific and detailed assessment and study of these relations might give new insight. To add another pain sensitivity task would increase an already longer experimental protocol. Since these questions were an aim of other ongoing studies from our lab, it was decided to not include further pain measures.

Moreover, the questionnaires selection could have been more specific to interoception concept. Maybe assessing strategies of emotional regulation such as those assessed by the Affect Intensity Measure questionnaire (AIM; Larsen RJ) would add knowledge regarding psychological dimensions that are related to interoception and regulation of emotions.

The comparisons in the current study were possible due to the new procedure: FAST. It is a novel paradigm based on an innovative perspective of pain assessment. Thus, further studies are needed to fully understand to what extend FAST is measuring specifically the ability to be accurate in pain reporting. Although it is still under investigation, assessing pain reporting accuracy may be considered controversial. It should be mentioned, however, that to argue about the relevance of this concept does not mean to deny the subjective nature of pain and to ignore that each subject reports his pain based on his specific and unique sensations. Yet, FAST has shown that part of the changes in pain reporting may occur due to other reasons, most probably related to the use of the pain scales. Using FAST it is possible to rule out those inaccuracies in order to identify the true differences in the pain the subjects' experience. This is a paradigm change and thus many other studies are needed to further validate this method and support these claims.

From a practical point of view, our results may have implications for clinical settings. If all the modalities are dissociable, individuals can be trained to become more accurate in a specific task, and that will not have repercussions in others. Moreover, different modalities may differently contribute for the general sense of the body and for some individuals it may be important to understand which modality may need to be improved. This may be relevant in chronic conditions, where deficits in interoception have been reported (for review see DiLernia, Serino & Riva, 2016). The possibility of identifying and modulate changes in a specific sensory channel was already tested in pain with good results. For example, in pain research, Treister (2018) has already showed that pain accuracy is a trainable skill by an evoked-pain training approach, which in turn reduces placebo response and accelerate the development of new treatment options.

Further studies from our lab are currently ongoing to continue investigating if the lack of relations between accuracy in different interoception modalities is also

found in clinical populations, particularly in chronic pain populations, where it has been consistently reported changes in interoception. Moreover, it is also interesting to assess the relation between the interoception modalities in populations known for their higher ability in perceiving bodily states, as dancers. This will give new insights regarding pain reporting skills.

Thus, knowing that the reporting of bodily signals is essential for emotional processing and for the expression of symptoms in several health conditions it is of the utmost importance to understand how to improve the ability to accurately report body signals and which individuals might be in needed of training for improving their ability to understand their subjective feelings and state of the body.

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5. Anexos

Anexo 1

CATÓLICA
INSTITUTO DE CIÊNCIAS DA SAÚDE
LISBOA·PORTO·VISEU

INSTITUTO DAS CIÊNCIAS DA SAÚDE DA UCP
COMISSÃO DE ÉTICA

Parecer 33/2017

Projecto de Mestrado em Neuropsicologia

Pain accuracy: Is There a Link Between Accuracy in Pain Report and Accuracy in Interception and Taste Tasks?

Mestranda: **Lic.ª Mariana Agostinho**

Orientadores: **Prof.ª Doutora Rita Canaipa**
Prof. Doutor Roi Treister

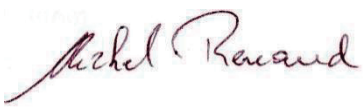
Na sua reunião de 3 de Abril de 2017, a Comissão de Ética do ICS da UCP tinha procedido à análise, numa perspectiva ética, do Projecto acima referido e tinha chegado à seguinte conclusão, comunicada no Parecer nº 31 de 24 de Abril:

«A Comissão considera que o Projecto de Investigação não levanta objecções de natureza ética. Apenas falta entregar o Curriculum Vitae da Candidata».

Este Curriculum Vitae foi devidamente entregue no dia 10 de Julho, de tal modo que se confirma que o Projecto de Investigação não levanta objecções de natureza ética.

Lisboa, 29 de Setembro de 2017

O Presidente da Comissão de Ética



Michel Renaud

Anexo 2

CONSENTIMENTO INFORMADO PARA PARTICIPAR NO ESTUDO

Relação entre a avaliação da dor e avaliação de estímulos de outras modalidades sensoriais

O presente estudo enquadra-se no projeto de Mestrado em Neuropsicologia pelo Instituto de Ciências da Saúde da Universidade Católica Portuguesa da licenciada Mariana Agostinho, sob a orientação científica da Profª Dra. Rita Canaipa do Centro de Investigação Interdisciplinar em Saúde do Instituto de Ciências da Saúde da Universidade Católica Portuguesa e do Prof. Dr. Roi Treister da Universidade de Haifa.

A sua participação neste estudo é inteiramente voluntária. Deve ler a informação que se segue e colocar questões sobre aquilo que não entender antes de decidir se participa ou não neste estudo.

Objetivos do Estudo

Este estudo tem como objetivo compreender os mecanismos de avaliação da dor em indivíduos saudáveis. É sabido que a avaliação da dor é muito subjetiva e que os estudos para desenvolver novos medicamentos e terapias têm dificuldade em compreender se as pessoas realmente conseguem revelar a dor que sentem. Este estudo tem, por isso, como objetivo compreender de que forma as pessoas avaliam a dor e se isso se relaciona com dificuldades na utilização das escalas de medição ou de particularidades na sua sensibilidade à dor noutras tarefas que não envolvem dor, como a frequência cardíaca e avaliação do paladar.

Procedimentos

Numa primeira fase, verificaremos se preenche todos os critérios clínicos necessários para a participação no estudo e pediremos a sua colaboração no preenchimento de alguns questionários que avaliam questões relacionadas com os seus hábitos de saúde e as suas emoções. Serão eles, um questionário sociodemográfico, a Escala Hospitalar de Depressão e Ansiedade e a Escala de Stress Percebido. Depois ser-lhe-á pedido que

participe em três tarefas. Uma tarefa envolve a avaliação da dor. Ser-lhe-ão aplicados estímulos térmicos de intensidade variável no seu braço, mas sempre em níveis adaptados à sua sensibilidade e considerados moderados, estímulos esses que deverá avaliar tendo em conta a intensidade que sentiu. A outra tarefa envolve a estimativa do seu batimento cardíaco, enquanto este é medido também por um medidor de cardiofrequência. Por fim, a última tarefa envolverá a avaliação do paladar, pela administração de soluções salinas e doces através de sprays.

Todos os estímulos aplicados durante o estudo terão intensidades variáveis, mas serão no máximo de dor moderada, **nunca atingindo níveis de dor intensa**. Estes estímulos são seguros, não implicando qualquer dano nos tecidos nem quaisquer consequências físicas ou emocionais a longo prazo**. PODERÁ PARAR A ESTIMULAÇÃO ASSIM QUE O ENTENDA**.

Interrupção da sua participação pelo investigador

Os investigadores podem ser forçados a interromper a sua participação neste estudo. Tal poderá acontecer se alguns procedimentos não se realizarem adequadamente, ou devido a inadequações das suas características, por razões de segurança ou por outras razões relevantes para o seu bem-estar ou para o bom desenvolvimento do projeto de investigação. Contudo, será sempre informado se essa situação se colocar.

Benefícios previstos do projeto de investigação

Este estudo pretende ajudar a esclarecer de que forma as pessoas avaliam a sua dor. Nesse sentido, os resultados obtidos poderão trazer informação importantes para estudos futuros que procurem desenvolver e testar novas terapias para o tratamento da dor. Contudo, deste estudo não se esperam benefícios diretos para o seu estado de saúde. Por outro lado, também não são de esperar quaisquer consequências negativas para o seu bem-estar físico ou psicológico.

Privacidade e Confidencialidade

As únicas pessoas que terão acesso à informação que nos fornecer serão os membros de investigação. Contudo, um código numérico ser-lhe-á atribuído para proteger a sua privacidade. Nenhuma informação sobre si será facultada a qualquer outra pessoa se não assinar consentimento escrito para tal.

Os dados serão analisados em conjunto para todos os participantes do estudo. Quando os resultados deste projeto de investigação forem publicados ou apresentados em conferências, não será fornecida qualquer informação que possa revelar a sua identidade.

Participação e desistência

A sua participação neste estudo em inteiramente **VOLUNTÁRIA**. Escolher participar ou não neste estudo não altera a sua relação com os investigadores nem com as instituições participantes. Se decidir participar poderá, no entanto, retirar o seu consentimento e desistir dessa participação em qualquer fase do estudo sem que tais relações se alterem.

Novos dados

Durante o curso do estudo será informado caso surjam novos dados que alterem os riscos ou benefícios da participação neste estudo e que, por consequência, possam implicar alterações na sua decisão sobre a participação neste projeto. Se tal ocorrer, ser-lhe-á pedido novo consentimento informado.

Identificação dos investigadores

Caso tenha alguma dúvida relacionada com o estudo ou necessite de entrar em contacto com os investigadores poderá fazê-lo para:

Lic. Mariana Agostinho mariana_ribolhos@hotmail.com ou pelo telemóvel 932679786

Prof. Dra. Rita Canaipa rita.canaipa@ics.lisboa.ucp.pt ou pelo telemóvel 966538648.

Assinatura do participante da investigação

Declaro que eu,_____

_____

_(nome) com o número de identificação _____ li e compreendi a informação relativa ao projeto de investigação acima. Foi-me dada a oportunidade de colocar questões, as quais foram devidamente esclarecidas. Foi-me dada uma cópia deste documento.

AO ASSINAR ESTE DOCUMENTO ASSUMO ACEITAR PARTICIPAR VOLUNTARIAMENTE NO ESTUDO NELE DESCRITO.

Assinatura:_____

_____

Data: _____

Assinatura do investigador

Expliquei o estudo ao participante e respondi a todas as suas questões. Considero que compreende a informação apresentada neste documento e consente livremente participar neste estudo.

_____ (nome do investigador)

Assinatura:

_____

Data: _____

Anexo 3

Questionário Sócio Demográfico

ID: __

Sexo

☐ Masculino

☐ Feminino

Idade: _____

Altura: _____

Peso atual: _____

Estado civil:
Solteiro

☐ Casado

☐ Casado ou viver em união de facto

☐ Separado ou Divorciado

☐ Viúvo

Qual o grau de ensino que completou?
Escolaridade ☐ nenhum ☐ 4ºano ☐ 6ºano ☐ 9ºano ☐ 12ºano ☐ Licenciatura ☐ Mestrado

Indique a data da sua última menstruação. _____

Medicação tomada nas últimas 48h. _____

Medicação que toma habitualmente. _____

Estilo de vida

Consome bebidas com cafeína (p.e. café, refrigerantes como coca-cola)?
Sim ☐
Não ☐
Se respondeu sim, quantas chávenas/copos toma por dia? _____
Quantas chávenas/copos consumiu nas últimas 48h? _____

Consome bebidas com teofilina e/ou bebidas energéticas (p.e. chá; red bull)?
Sim ☐
Não ☐
Se respondeu sim, quantas chávenas/copos toma por dia? _____
Quantas chávenas/copos consumiu nas últimas 48h? _____

Consome bebidas alcoólicas?
Sim ☐
Não ☐
Se respondeu sim, quantos copos toma por dia? _____
Quantos copos consumiu nas últimas 48h? _____

Fuma?
Sim ☐
Não ☐
Se respondeu sim, quantos cigarros fuma por dia? _____
Quantos cigarros fumou nas últimas 48h? _____

Consome drogas recreativas?
Sim ☐
Não ☐
Se respondeu sim, quantos consumos faz por semana? _____
Quantos consumos fez nas últimas 48h? _____

Faz exercício físico com regularidade?
Sim ☐
Não ☐
Se sim, quantas vezes por semana?_____
Qual a duraçãode cada sessão/treino? _____
Quantas horas de exercício físico fez nas últimas 48h?_____

É predominantemente
Dextro ☐
Canhoto ☐

Acontecimentos prévios que tenham resultado em queimaduras severas?

_____

História de dor crónica?

_____

Anexo 4

אוניברסיטת חיפה
University of Haifa
جامعة حيفا

הפקולטה למדעי הרווחה והבריאות

Faculty of Social Welfare & Health Sciences

الكلية لعلوم الرفاه والصحة

Research Protocol

Experiment instructions

In this experiment, you will receive heat stimuli through thermal probe that will be attached to the dorsal aspect of your forearm. It is important to notify that all devices and stimuli given to you during this experiment are approved and safe to use, and should not cause any physical harm. You may have slight redness in the stimulated area that will disappear within a few minutes to hours from the end of the experiment.

In this experiment, we will focus on the intensity of the pain you experience following stimulation - if you feel pain at all. You will be asked to rate your pain on a 0-100 scale; where "0" is "no pain", and "100 is your "worst imaginable pain".

The goal in this experiment **is not** to test your pain tolerance level, but it is very important to understand the whole scale in order to give proportional ratings of the intensity of the pain you are experiencing. Since this scale refers to **pain** sensation solely, any other sensation beside pain - such as warmth, tingling, tickling etc., will be **defined as "0"**. It is important to mention that there is no wrong answer, and every number (i.e. 24, 73, 6, 41) which you think reflects your perceived pain intensity is right.

You will be asked to rate the pain intensity based on this scale at different time points in which you will be asked to do so. Please provide a quick and accurate respond that will reflect your perceived pain.

At any stage, you can ask to cease the stimulation or to finish the experiment and your request will be answered immediately. Because the probe is very sensitive, we ask you not to touch it.

Familiarization stage:

- 3 executive stimuli from 44°C, 46°C, and 49°C, each lasting 3 seconds –**DOMINANT ARM**

Instructions to the subject: "In this stage, we aim to familiarize you with the different devices and stimuli you will feel during the test. You are about to receive several short heat stimuli to your forearm. The heat stimuli will be given through this probe (show the subject). All stimuli or some will cause painful sensation. When given the cue word **"now"**, you will be asked to rate your maximal perceived pain. I remind you to use the scale of 0-100, "0" is "no pain", and "100 is the "your worst imaginable pain".

- **Important** – between each stimulus to adjust the probe to a new area on the arm

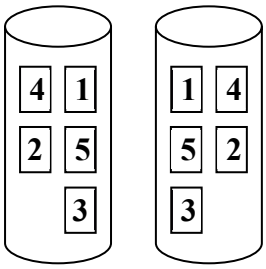
- **5 minutes brake.**

FAST

- 49 executive stimuli ranging from 44°C to 50°C, each lasting 3 sec- **NON_DOMINANT ARM**

Instructions to the subject: "You are about to receive several short heat stimuli to your forearm. When given the cue word **"now"**, you will be asked to rate your maximal perceived pain. I remind you to use the scale of 0-100, "0" is "no pain", and "100 is the "your worst imaginable pain. It is very important that you will stay focused and try to be as accurate in your pain ratings as possible".

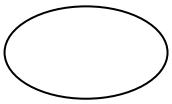
- **Important** – every 10 stimuli adjust the probe to a new area on the arm according to the picture:



Anexo 5

Registration Sheet

Tester name: Subject name: Date: Subjects no.:



רצף A

Pain Assessment - TSA

Training Phase - TSA:

Familiarization – TSA:

Temperature	46.5°C	44°C	48°C
NPS			

FAST:

°C	NPS	°C	NPS	°C	NPS	°C	NPS	°C	NPS

Anexo 6

Taste Task (Hendi and Leshen, 2014)

Preparation of sprays

When preparing the sprays, wash the flasks and the sprays well. And this is because low concentrations of sugar can develop fungi and therefore must be careful hygiene and weekly exchange of sprays. After filling all the sprays, check that each bottle is sprayed properly by a few clicks. Always make sure that the spray is done when the bottle is upright.

Figure 1 is the vial illustration used for this experiment.

Figure 1. Example of vials used in the study

How to prepare the sprays

The procedure for the preparation of the sprays will be performed according to the weight / volume ratio of W / V, according to solid grams per liter of liquid.

The preparation will be done according to the method of dilution of each concentration in order to receive the next concentration, from a high concentration to a lower concentration.

In order to prepare the sprays, mineral water will be used with a maximum of 9 mg / L.

This procedure originally developed to assess the sensitivity to salty and sweet taste was modified to assess reporting accuracy of tastes (Hendi and Leshen, 2014). The exact ratio of concentrations was determined based on a previous pilot study aimed to identify concentrations that will be perceived, on average, as distinct from each other. Herein we determined a new solution (vial 4) in our lab, described in the table 1.

Protocol Spray Accuracy Project (Mariana, Rita, Liat & Roi).

	vial 5	vial 4	vial 3	vial 2	vial 1
Salt	37.5 g / 250cc (100ml no frasco)	1:5	1:3	1:3	1:3
Sugar	67.5 g / 250cc	1:1	1:2	1:2	1:2

Table 1. Dilution preparation. Ratios of concentration.

These ratios of concentration are achieved by the following preparation.

Salt

Vial 5: add 37.5g to 250cc. Of this concentration, add 100ml to the vial.

Vial 3: to 100ml of the surplus from the previous solution add 300ml of water.

Vial 2: to 100ml of the surplus from the previous solution add 300ml of water.

Vial 1: to 100ml of the surplus from the previous solution add 300ml of water.

Vial 4: repeat procedure for vial 5. Then to 100ml of the surplus of the previous solution add 150ml.

Sugar

Vial 5: 67.5 g / 250cc. Of this concentration, add 100ml to the vial.

Vial 3: to 100ml of the surplus from the previous solution add 200ml of water.

Vial 2: to 100ml of the surplus from the previous solution add 200ml of water.

Vial 1: to 100ml of the surplus from the previous solution add 200ml of water.

Vial 4: repeat procedure for vial 5. Then to 100ml of the surplus from the previous solution add 100ml of water.

Procedures for application:

1. Before splashing into the mouth, the vial must be carefully shaken, and a single shot should be carried into a glass or napkin to fill the straw of the vial. The spray is always done when the bottle is vertical. When spraying, press the spray button firmly, all the way down. Do not touch the vial of sprays in your lips, mouth, or tongue to maintain the hygiene of aerosols (distance of 1.5 cm).
2. Make sure that the product tastes best (open mouth, tongue inside). Make sure that the bottle is always vertical in the spray so that the bottle tube will not enter the air and the volume of the spray will change. The experimenter will spray the spray directly into the centre of the oral cavity - the goal is to cover the entire oral cavity, not just the tongue. A uniform spray pattern should be observed for all subjects: only one spray when the bottle is completely vertical, and the entire spray solution enters the mouth. If one thesis misses, write down its number and repeat it at the end of the set. For this purpose, return to the spray number that has been missed and re-spray (in the new software).
3. After each taste, the subject will rinse his mouth with mineral water.
4. Always keep track of the subjects' ratings and see that they do not rank "just". If there is such a concern, raise his attention to the task.

Instructions:

In this task we will examine your sensitivity to the palate.

Here are vials with 7 different concentrations of each flavour that we want you to evaluate. We will show you the sprays in random order and spray the contents of the vials into your oral cavity. For each spray we ask your help to rate from 0 to 100: if the intensity is do not feel/weak "0" to "100" very strong. Then wash your mouth with a little water to prevent residual taste from interfering with the next taste. Try to perform the task with care and attention so that the results are correct and accurate. If any information is less clear, please ask whenever you need it.

Anexo 7

Instruções em Português

Tarefa de dor: Instruções FAST

Nesta experiência, irá receber estímulos de calor através de uma sonda térmica que será colocada na parte dorsal do seu antebraço. É importante referir que todos os dispositivos e estímulos que lhe são dados durante esta experiência são aprovados e seguros para uso e não devem causar qualquer dano físico. Pode ter uma leve vermelhidão na área estimulada que desaparecerá dentro de alguns minutos a horas após o final da experiência.

Nessa experiência, vamos focar-nos na intensidade da dor que você experiencia após a estimulação – isto se sentir dor de alguma forma. Será pedido para avaliar a sua dor numa escala de 0-100; onde "0" é "sem dor", e "100 é a sua" pior dor imaginável ".

O objetivo nesta experiência não é testar seu nível de tolerância à dor, mas é muito importante que entenda toda a escala para obtermos classificações proporcionais da intensidade da dor que está a sentir (experienciar). Uma vez que esta escala se refere apenas à sensação de dor, qualquer outra sensação além de dor - como calor, formigueiro, cócegas etc., será definida como "0". É importante mencionar que não há uma resposta errada, e cada número (ou seja, 24, 73, 6, 41) que pense que reflete sua intensidade de dor percebida é certo.

Será solicitado a avaliar a intensidade da dor com base nesta escala em diferentes momentos quando lhe for pedido que o faça. Por favor, forneça uma resposta rápida e precisa que reflita a sua dor percebida.

Em qualquer fase, pode pedir para parar a estimulação ou terminar a experiência e seu pedido é respondido de imediato. Para além disto, como a sonda é muito sensível, pedimos que não lhe toque.

Etapa de familiarização:

• 3 estímulos consecutivos a partir de 44 ° C, 46 ° C e 49 ° C, cada um com duração de 3 segundos.

Braço dominante

Instruções "Nesta fase, pretendemos familiarizá-lo com os diferentes dispositivos e estímulos que sentirá durante o teste. Está prestes a receber vários estímulos curtos de calor no seu antebraço. Os estímulos de calor serão aplicados através desta sonda (mostrar). Todos os estímulos ou alguns vão causar sensação dolorosa. Quando receber a palavra-chave "agora", será pedido que avalie sua dor máxima percebida. Lembro-lhe que use a escala de 0-100, "0" é "sem dor", e "100 é a" pior dor imaginável ".

• Importante - entre cada estímulo para ajustar a sonda a uma nova área no braço

• 5 minutos de repouso

Fast

• 49 estímulos consecutivos variando de 44 ° C a 50 ° C, cada um com duração de 3 seg.

Braço não dominante

Instruções: "Está prestes a receber vários estímulos curtos de calor no seu antebraço. Quando ouvir a palavra" agora ", será pedido que avalie a sua dor máxima percebida. Lembro-lhe que use a escala de 0 a 100 "0" é "sem dor", e "100 é a" pior dor imaginável. É muito importante que se mantenha focado e tente ser tão preciso quanto possível nas classificações de dor ".

• Importante: cada 10 estímulos ajustam a sonda a uma nova área no braço de acordo com a imagem:

Tarefa de Paladar

Nesta tarefa vamos examinar a sua sensibilidade ao paladar.

Aqui estão frascos com 7 concentrações diferentes de cada sabor que pretendemos que avalie. Vamos mostrar-lhe os sprays em ordem aleatória. Vou pulverizar para a sua cavidade oral o conteúdo dos frascos. Para cada spray pedimos a sua ajuda para nos classificar de 0 a 100 qual a intensidade: se a intensidade é não sinto/fraco "0" até "100" muito forte. Depois peço que enxague a sua cavidade oral com um pouco de água, que pode deitar fora para um copo vazio ou pode engolir. O objetivo é prevenir que sabor residual interfira no próximo sabor. Tente realizar a tarefa com cuidado e atenção para que os resultados sejam corretos e precisos. Se alguma informação estiver menos clara, por favor pergunte sempre que precisar.

Tarefa de Interocepção

Nesta tarefa pretendemos avaliar a sua interocepção, isto é, a sua perceção ou sensibilidade em relação a estímulos e variações de processos fisiológicos internos.

Para isto, iremos utilizar este aparelho para registar a sua frequência cardíaca e respiração. Mostrar. Vamos realizar um ECG e vamos colocar os elétrodos segundo o triângulo de Eithoven, quer isto dizer que vamos colocar o elétrodo terra no seu ombro esquerdo, o elétrodo positivo perto da sua crista ilíaca.

Nesta tarefa pedimos que tente contar o número de batimentos cardíacos durante os períodos de tempo que lhe vou indicando, concentrando-se apenas em sensações corporais. Não pode sentir o pulso ou a tentar outro tipo de manipulação física que possa facilitar a deteção. Ao sinal sonoro "agora" pedimos que comece a contar o número de batimentos cardíacos silenciosamente e que quando ouvir a palavra "stop" nos diga o número ou estimativa dos batimentos cardíacos que contou. Inicialmente iremos começar com alguns minutos em repouso e quando ouvir a palavra "agora" pode começar. Irá realizar esta tarefa algumas vezes, intercalada com períodos de repouso, pelo que pedia que estivesse muito concentrado. É muito importante que se mantenha o mais imóvel possível, evitando movimentos bruscos. Isto ajudará a sua contagem e permitirá uma melhor recolha de dados.

Quando ouvir a palavra "agora" comece a contar os batimentos cardíaco até ouvir "stop".

Anexo 8

Supplementary figures

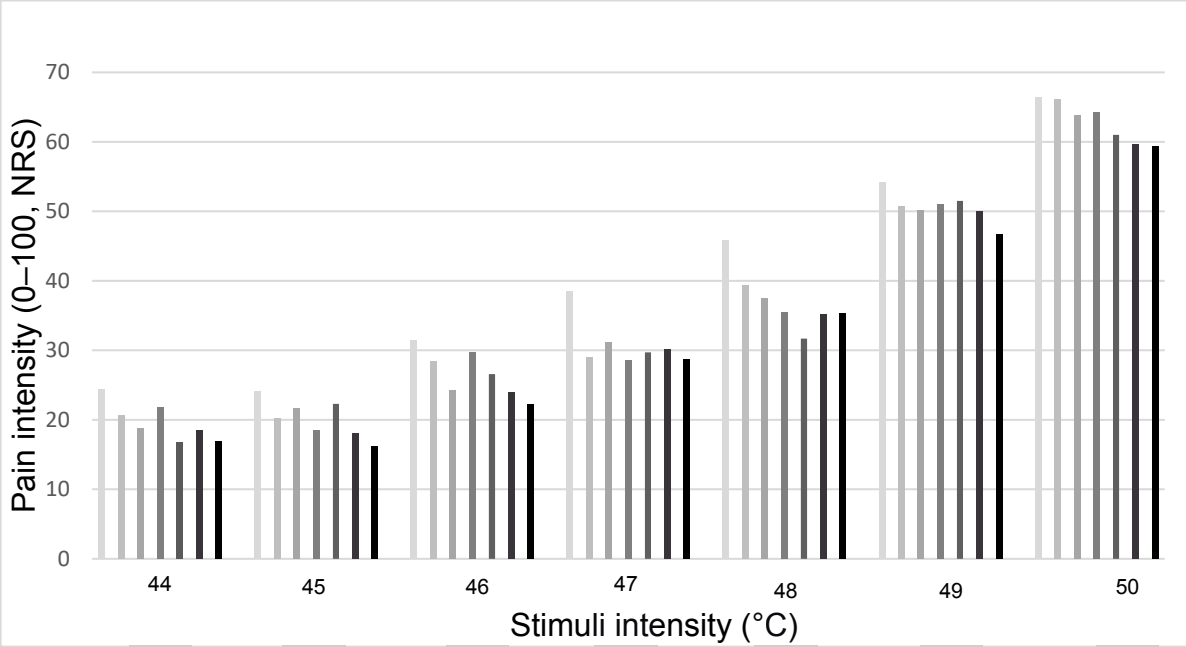


Figure 1 Mean pain scores in response to the 49 focused analgesia selection test stimuli by stimulus order.

Note: For each stimulus intensity, the 7 bars represent the 7 repetitions of stimuli for each intensity, organized by order. The lighter bar on the left represents the first stimulus and the black bar on the right the 7th stimulus.

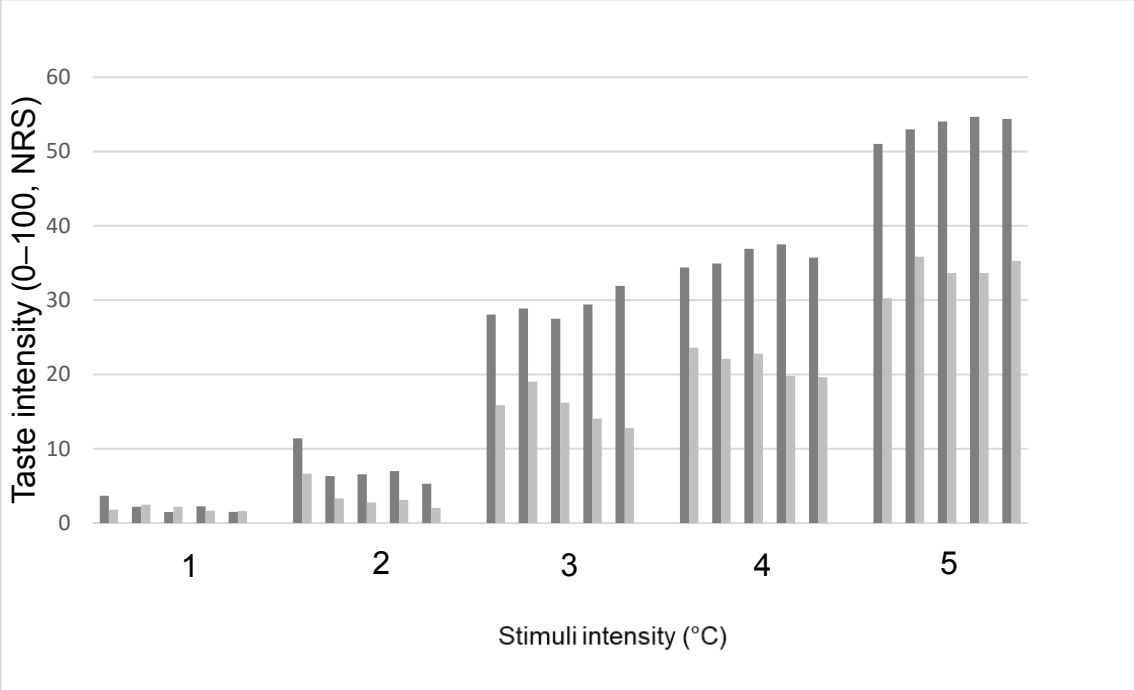


Figure 2 Mean taste scores in response to the 25 salt and sugar stimuli by stimulus order.

Note: For each stimulus intensity, the 5 bars represent the 5 repetitions of stimuli for each intensity, organized by order. The darker bars on the left represents the salt stimuli from the first stimulus to the 5th stimulus and the lighter bars on the right represent the sugar stimuli from the first stimulus to the 7th stimulus.

Anexo 8

Presence in conferences and meetings

ASP's 17th World Congress on Pain from September 12-16, 2018, in Boston, Massachusetts at the Boston Convention & Exhibition Center (BCEC).

Poster presentation (see poster next page)

Poster Number: PTH254
Poster Abstract Title: Pain Reporting Accuracy: Is There a Link Between Accuracy of Pain Report and Accuracy of Reports of Other Sensations?
Presentation Date: Thursday, September 13
Presentation Time: 9:30 AM - 10:30 AM

Poster Reference:

Agostinho, M., Canaipa, R., Honigman, L. & Treister, R. (2018). Pain Reporting Accuracy: Is There a Link Between Accuracy of Pain Report and Accuracy of Reports of Other Sensations? 17th World Congress on Pain. Boston, September 13, 2018.

Pain reporting accuracy does not correlate with ability to accurately report other bodily sensations

Agostinho, Mariana[1]; Canaipa, Rita[1]; Honigman, Liat[2]; Treister, Roi[2]

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Introduction

- Despite of the high prevalence and burden of pain, there is still lack of adequate pain treatments and medications. In part this may be due to low assay sensitivity of analgesic clinical trials, attributed to the high variability of the participants' pain scores.
- Recently the Focused Analgesia Selection Test (FAST) was developed and validated to measure patients' pain reporting skills, allowing for the first time to assess how accurate subjects are in reporting their pain. However, little is known about this skill [1], and it is unknown if accuracy in pain report is a pain-specific ability, or represent a general ability to accurately assess and report sensations of other sensory modalities.
- Interoceptive signals ascend from the periphery in two main pathways, the spinothalamical and lemniscal tracts [2], integrated at multiple levels, among which the medial and the anterior insular cortex play the primary role [3]. Given that interoceptive information, regardless of its origin, is processed by same brain structures, it is reasonable to speculate that being able to accurately report pain will correlate with ability to accurately report other sensations.
- Herein, we evaluate pain report accuracy and its correlation with the ability to accurately report other sensations, specifically to accurately detect heartbeat and tastes.

Materials and Methods

- Healthy volunteers were enrolled from local universities, underwent the FAST procedure which assesses pain reporting accuracy (by calculating the R2 value of relations between pain reports and stimuli intensities) in response to repeated administration of thermal noxious stimuli of varying intensities.
- Interoception accuracy (IA) was evaluated by the "Mental Tracking Method" (Schandry's task) which is based on concordance between subjective and objective heart beat counting [4]. The overall score was calculated according to the formula:

  IAc score= 1/3∑[1-(recorded heartbeats - counted heartbeats) / recorded heartbeats].
- Taste Task Accuracy measured the accuracy (R2) reporting salty and sweet tastes of various concentrations [5]. During the task, the experimenter sprayed each taste solution onto the participant's oral cavity in a semi-randomised order. Between every two sprays subjects were requested to drink a sip of water in order to wash their oral cavity. Each concentration was repeated 5 times (a total of 25 repeats for each taste).
- The participants were asked to indicate the intensity or how strong was the flavor, for each concentration of taste on a numerical rating scale ranging from 0 "not feeling", to 100 "most strong".
- Participants also completed the Perceived Stress Scale, Hospital Anxiety and Depression Scale, and the Multidimensional Assessment of Interoceptive Awareness (MAIA).

Results

Participants' Characteristics

- Participants characteristics are summarized in table 1 and scores in psychological questionnaires in table 2.
- The study sample included 60 volunteers (29 men and 31 women), with mean ± standard deviation (SD) of 23.63 ± 6.31 years.

Characteristics	Mean ± SD	Frequency (%)	Range
BMI (Kg/m)	22.7 ± 3.5		14.1-32.7
Education			
High school		40 (66.7%)	
Undergraduate		15 (30%)	
Graduate		2 (3.3%)	
Marital Status			
Single		56(93.3%)	
Married		4(4.7%)	

Table 1. Subjects' demographic characteristics

Questionnaires	Mean ± SD	Median
PSS	18.45 ± 7.15	18.0
HADS-total	11.05 ± 6.10	9.0
HADS-anxiety	7.05 ± 3.55	7.0
HADS-depression	3.95 ± 3.22	3.0

Table 2. A summary of the the psychological questionnaires. Abbreviations: PSS, perceived stress scale; HADS, hospital anxiety and depression scale.

FAST outcome measures

- Figure 1 illustrates the FAST results of 2 representative subjects; subject A who demonstrated low variation in his pain reports ("accurate" pain reporter), and subject B who demonstrated high variability in his pain reports ("non-accurate" pain reporter). In these figures, each dot represents 1 rating of 49 stimuli administrated at 7 intensities.
- Table 3 summarizes the FAST outcomes of reporting accuracy.

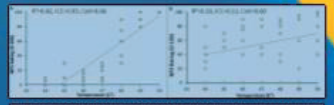

Figure 1. Examples of FAST results obtained for a (A) "accurate" vs. (B) "non-accurate" pain reporter.

	R^2	ICC	CoV
Mean (SD)	0.493 (0.18)	0.602 (0.16)	0.577 (0.38)
Median	0.49	0.62	0.49
Minimum	0.01	0.08	0.05
Maximum	0.77	0.87	1.36

Table 3. FAST Outcomes. Abbreviations: R2, power model regression; CoV, coefficient of variation; ICC, intraclass correlation coefficient; SD, standard deviation.

Interoception outcome measures

- The mean heartbeat perception score was 0.65 (range 0.00–0.98), with median score of 0.69 (table 4).
- This scores suggest that participants differ in their interoception accuracy, assessed by the Schandry's task.
- Table 5 depicts the results of the Multidimensional Assessment of Introceptive Awareness (MAIA) questionnaire.

Interoception Task	
Mean (SD)	0.65 (0.23)
Median	0.69
Minimum	0
Maximum	0.98

Table 4. Heartbeat perception score

MAIA sub-scales	Mean ± SD	Median	Min-Max
Noticing	3.58 ± 0.9	3.33	0-5
Not Distracting	1.66 ± 0.9	1.50	0-4.3
Not worrying	2.70 ± 1.1	3.0	0.25-5
Attention Regulation	3.02 ± 0.8	3.0	1.14-4.71
Emotional Awarenss	3.84 ± 0.8	3.60	1.80-5
Self-Regulation	2.87 ± 0.9	2.57	1-4.43
Trusting	3.81 ± 0.8	4.0	1.67-5
TOTAL	3.44 ± 15.7	2.91	1.33-95

Table 5. Multidimensional Assessment of Interoceptive Awareness questionnaire

Taste task outcome measures

- Mean taste intensity ratings reported in response to each of the five concentrations for both sugar and salt are presented in Figure 2.
- Taste task accuracy outcomes are described in tables 6.

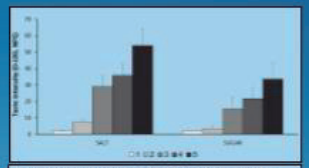

Figure 2. Each bar represents the average taste scores in response to the different salt/sugar concentrations. Error bars represent the standard error of the mean.

SALT	R^2	ICC	CoV
Mean (SD)	0.666 (0.14)	0.831 (0.12)	0.475 (0.21)
Median	0.72	0.88	0.44
Minimum	0.24	0.17	0.12
Maximum	0.92	0.96	0.88
SUGAR	R^2	ICC	CoV
Mean (SD)	0.614 (0.18)	0.774 (0.15)	0.496 (0.22)
Median	0.65	0.81	0.47
Minimum	0.09	0.06	0.09
Maximum	0.87	0.96	1.12

Table 6. Taste task outcomes.

Associations between accuracy tests from different modalities

- The only association was found between reporting accuracy of the two tastes. Subjects with high salt ICC had a high sugar ICC values (Spearman's r=0.477, P<0.001).
- No significant cross-modal correlations were found between any of the accuracy tasks (FAST, heartbeat task and taste) (P>0.05 for all outcome measures).
- Interoception task did not significantly correlate with the measures assessed by the MAIA questionnaire.
- Accuracy in different tasks was not correlated to stress, psychological symptoms, or Interoception Awareness, assessed by MAIA.

Conclusions

- Our results suggest that interoceptive accuracy covary across different modalities [6-9]. In line with our findings, a recent study also found correlations within measures of the same sensory modality, but not between modalities [8].
- Aligned with previous research, interoception tasks did not significantly correlate with the measures assessed by the MAIA questionnaire, indicative that these tasks do not measure the same constructs [6].
- Based on a recent model [10], interoception is processed by three hierarchical systems: the "generative", processing information from each sensory system (involving somatosensory cortex and posterior insula), the "perceptual", where a first "whole-body pattern" is constructed (in the anterior insula) and the "regulatory", the final stage (integrating the anterior cingulate cortex) where the emotional concepts are created using information from the lower level processing with higher systems. Based on this model the results of the current study suggest that each sensory modality is independently processed before integration to generate a more general "whole-body" assessment.

In summary, the current study demonstrated lack of associations between pain reporting accuracy and the accuracy of reporting other sensations, suggesting that interoceptive accuracy cannot be generalized to other modalities. Treister (2018) [11] has recently showed that pain accuracy is a trainable skill that can be improved by an evoked-pain training approach. The lack of correlations between accuracy reporting of various modalities found in this study suggest that improving reporting accuracy of one modality will probably not affect the accuracy reporting of other modalities.
Further investigation is needed in order to understand differences in the accuracy in symptom reporting and its clinical relevance.

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[11] Treister et al PLOS ONE 2018;13(5):e0197844.

Acknowledgments
We wish to thanks Neuroser (http://neuroser.pt/) and particularly Dra Ana Paula Silva for providing the place in which data collection was performed.

Anexo 9

Presence in Meetings

The first meeting on Pain Reporting Accuracy

AGENDA

September 16, 2018 (1-5 PM)

Time	*Topic*	*Speaker*
1:00 - 1:30	**Meeting, greeting, and lunching**	
1:30 - 1:45	Pain reporting accuracy - Historical perspective	Nathaniel Katz, MD, Tufts University, Analgesic Solutions
1:45 - 2:15	Overview on previous research	Roi Treister, PhD University of Haifa
2:15 - 2:30	Pain reporting accuracy and interceptive awareness	Mariana Agostinho, Master student, Universidade Católica Portuguesa
2:30 - 2:50	Pain reporting accuracy in Fibromyalgia patients	Rita Canaipa,PhD Universidade Católica Portuguesa

Time	*Topic*	*Speaker*
2:50 - 3:00	Pain reporting accuracy and the placebo response	Liat Honigman, PhD University of Haifa
3:00 - 3:15	Update on on-going studies	Liat Honigman, PhD University of Haifa
3:15 - 3:30	**Coffee/Bio brake**	
3:30 - 4:00	Pain reporting accuracy, variability of pain reports and the placebo response – a conceptual model	Roi Treister, PhD University of Haifa
4:00 - 4:45	Future directions –open discussion	All together

END OF MEETING

Speaker Attendees:

Nathaniel Katz, MSc, MD, CEO of Analgesic Solutions and Department of Anesthesiology and Perioperative Medicine, Tufts University School of Medicine, Boston, MA.

Mariana Agostinho, BSc , CIIS, Centro de Investigação Interdisciplinar em Saúde, Instituto de Ciências da Saúde, Universidade Católica Portuguesa

Rita Canaipa, PhD , CIIS, Centro de Investigação Interdisciplinar em Saúde, Instituto de Ciências da Saúde, Universidade Católica Portuguesa

Liat Honigman, PhD, Director, The Clinical Pain Innovation Lab, Faculty of Social Welfare and Health Sciences, University of Haifa, Haifa, Israel.

Roi Treister, PhD, Head, The Clinical Pain Innovation Lab, Faculty of Social Welfare and Health Sciences, University of Haifa, Haifa, Israel.

Anexo 9

Boston Presentation at “The first meeting on Pain Reporting Accuracy”

PAIN REPORTING ACCURACY DOES NOT CORRELATE WITH ABILITY TO ACCURATELY REPORT OTHER BODILY SENSATIONS

Agostinho, Mariana

Master Student

CIIS, Centre for Interdisciplinary Health Research, Institute of Health Sciences,

Catholic University of Portugal, Lisbon, Portugal.

INTRODUCTION

Pain intensity, as intensities of other subjective experiences is challenging to measure.

Recent findings show subjects vary in their ability to **accurately** report pain, and this predicts the ability to accurately report changes in clinical pain (Treister, 2017).

Focused Analgesia Selection Test (FAST)

PAIN REPORTING ACCURACY

INTRODUCTION

INTEROCEPTION

"the sense of the physiological condition of the entire body"

Pain - Temperature - Cardiorespiratory function - Hunger - Thirst - Stress

(Craig, 2002,2009)

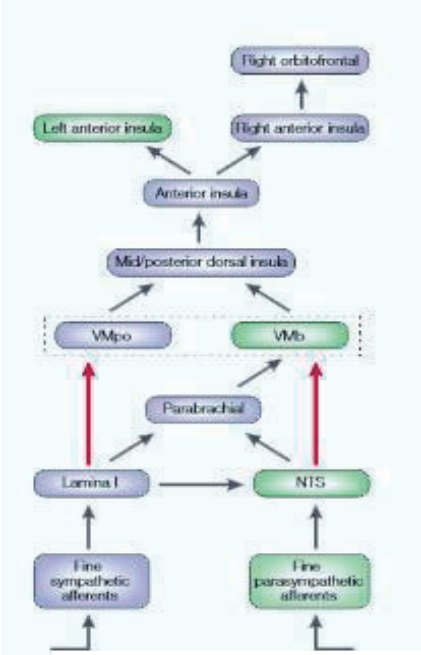


Figure 1. Organizational chart for interoception; nucleus of the solitary tract (NTS); ventromedial thalamic nucleus (VMb); ventromedial nucleus (VMpo).

Multichannel Investigation of Interoception: Sensitivity Is Not a Generalizable Feature

Eszter Ferentzi[1,2], Tamás Bogdány[2], Zsuzsanna Szabolcs[1,2], Barbara Csala[1,2], Áron Horváth[2,3] and Ferenc Köteles[2]*

[1]Doctoral School of Psychology, ELTE Eötvös Loránd University, Budapest, Hungary, [2]Institute of Health Promotion and Sport Sciences, ELTE Eötvös Loránd University, Budapest, Hungary, [3]Institute of Psychology, ELTE Eötvös Loránd University, Budapest, Hungary

Objective: The term interoception refers to the perception of bodily cues. In empirical studies, it is assessed using heartbeat detection or tracking tasks, often with the implicit assumption that cardioception reflects general interoceptive ability. Studies that applied a multichannel approach measured only a limited number of modalities. In the current study, six modalities were assessed to gain a deeper understanding of the relationship between the different sensory channels of interoception.

Methods: For 118 university students (53% male) gastric perception (water load test), heartbeat perception (Schandry task), proprioception (elbow joint), ischemic pain (tourniquet technique), balancing ability (one leg stand), and perception of bitter taste were measured. Pair-wise correlation analysis and exploratory factor analyses (principal component analysis (PCA) and maximum likelihood (ML) extraction with oblimin rotation) were then carried out with a three-factor solution to investigate the underlying associations.

Results: Correlation analysis only revealed significant associations between variables belonging to the same sensory modality (gastric perception, pain, bitter taste). Similarly, the three factors that consistently emerged in the factor analyses represented the three aforementioned modalities.

Discussion: Interoceptive sensitivity assessed by using one channel only cannot be generalized. Interoceptive modalities carrying crucial information for survival are not integrated with other channels.

Keywords: interoception, interoceptive sensitivity, heartbeat perception, pain, water load test, balance, bitter taste

INTRODUCTION

Methodological differences that can account for the contrasting findings in Ferentzi study:

- It involved different sensory channels and different task modalities.
- Pain was measured using a threshold and tolerance tasks, measures assessing pain sensitivity.
- A single VAS score of intensity (or unpleasantness) of a taste solution was used to assess the sensitivity of subjects to a given taste.

AIM

An open question is whether accuracy in pain reporting is a "general" skill, or is it a pain specific phenomena:

- We aimed to explore if the ability to accurately report pain is correlated with the ability to accurately report other bodily sensations.

PAIN	*HEARTBEAT*	TASTE

METHODS

Subjects: Healthy subjects

Procedures:

- FAST
- **Introceptive accuracy (IA)**
- **Taste perception task**

Questionnaires:

- Perceived Stress Scale (PSS): brief instrument, used in community samples to assess stress in daily life situations during last month
- Hospital Anxiety and Depression Scale (HADS): brief instrument commonly used to assess anxiety and depression in non-psychiatric population
- **Multidimensional Assessment of Interoceptive Awareness (MAIA)**

HEARTBEAT PERCEPTION TASK

Mental Tracking Method assesses the individuals' ability to be accurate in the perception of its heartbeat (Schandry's task, 1981).

Instructions:

"Without manually checking, count silently each heartbeat you feel in your body from the time you hear "start" to when you hear"stop". Avoid any kind of physical manipulation (pressure points, respiratory manipulation) that might ease detection".

Baseline (5min) - rest (60s) - familiarization (10s) - rest (60s) - **perception (25s)** - rest (30s) - **perception (35s)** - rest (30s) - **perception (45s)** - rest (60s).

IA score= $\frac{1}{3}\sum[1-(recordedheartbeats-countedheartbeats)/recordedheartbeats]$

IA vary between 0 - 1. Higher scores indicate better IA.

Figure 2. BITalino device, Plux Wireless Biosignals, SA, Lisbon, Portugal

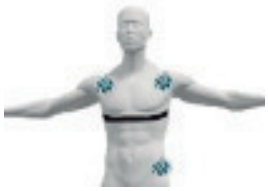


Figure 3. Electrodes placement: Einthovens' triangle. Respiratory belt.

TASTE PROTOCOL

- This procedure originally developed to assess the sensitivity to salty and sweet taste was modified to assess reporting accuracy of tastes (Hendi and Leshen, 2014). The exact ratio of concentrations was determined based on pilot studies aimed to identify concentrations that will be perceived, on average, as distinct from each other.

	vial 5	vial 4	vial 3	vial 2	vial 1
Salt	37.5 g / 250cc	1:5	1:3	1:3	1:3
Sugar	67.5 g / 250cc	1:1	1:2	1:2	1:2

Table 1. Dilution preparation. Mineral water with a maximum of 9 mg NaCl/ L.

Figure 4. Example of vials used in the study.

TASTE PROTOCOL

Procedure:

1. The participants were asked to avoid eating, drinking (except water) and smoke 2 hours before the test.
2. Researcher sprayed each vial onto the participants' oral cavity in a semi-randomised order.
3. The participants were asked to indicate how strong was the flavour, for each concentration of taste, on a numerical rating scale ranging from 0 "not feeling", to 100 "most strong".
4. Between every two sprays subjects were requested to wash their oral cavity with mineral water.
5. Each concentration was repeated 5 times (a total of 25 repeats for each taste).

Taste outcomes: R^2, ICC and CoV

MAIA

Noticing

1. When I am tense I notice where the tension is located in my body.
2. I notice when I am uncomfortable in my body.

Not-distracting

6. I distract myself from sensations of discomfort.
7. When I feel pain or discomfort, I try to power through it.

Not-worrying

8. When I feel physical pain, I become upset.
9. I start to worry that something is wrong if I feel any discomfort.

Attention Regulation

14. I can return awareness to my body if I am distracted.
15. I can refocus my attention from thinking to sensing my body.
16. I can maintain awareness of my whole body even when a part of me is in pain or discomfort.

Emotional Awareness

21. I notice that my breathing becomes free and easy when I feel comfortable.
22. I notice how my body changes when I feel happy / joyful.

Self-Regulation

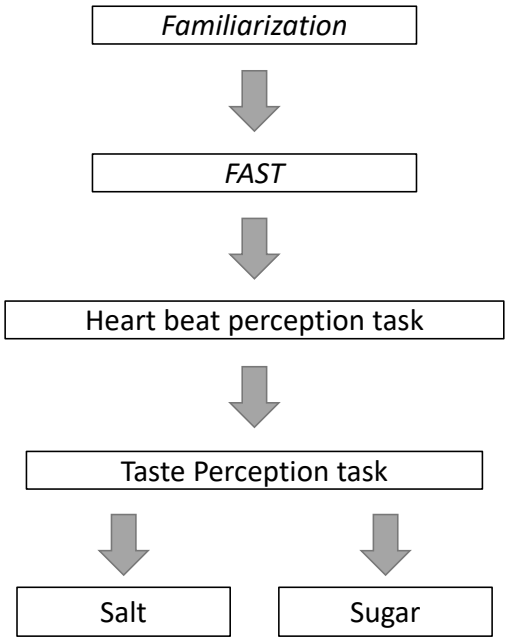
24. When I bring awareness to my body I feel a sense of calm.
25. I can use my breath to reduce tension.
26. When I am caught up in thoughts, I can calm my mind by focusing on my body/breathing.
27. I listen for information from my body about my emotional state.
28. When I am upset, I take time to explore how my body feels.

Trusting

31. I feel my body is a safe place.
32. I trust my body sensations.

Figure 5. Few examples of MAIA items for each scale. Original version by Mehling, 2012. Portuguese version by Machorrinho, 2017.

EXPERIMENTAL PROTOCOL



RESULTS

- 60 volunteers, 29 men and 31 women (mean ± standard deviation (SD): 23.63 ± 6.31 years).

Characteristics	Mean ± SD	Frequency (%)	Range
BMI (Kg/m)	22.7 ± 3.5		14.1-32.7
Education			
High school		40 (66.7%)	
Undergraduate		18 (30%)	
Graduate		2 (3.3%	
Marital Status			
Single		56 (93.3%)	
Married		4 (6.7%)	

Table 1. Demographic characteristics.

RESULTS

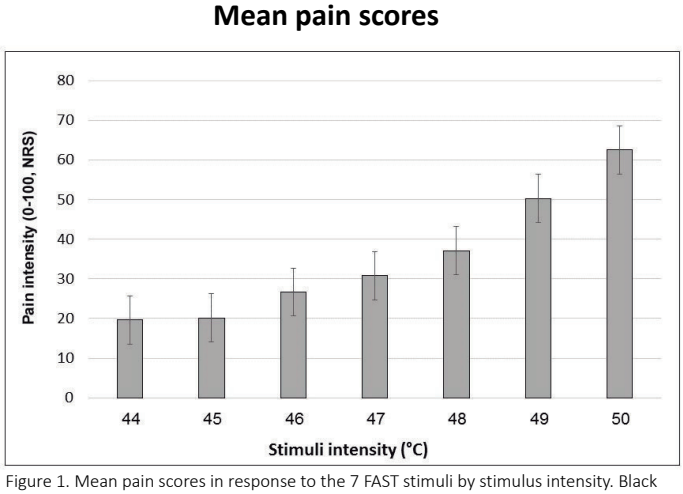


Figure 1. Mean pain scores in response to the 7 FAST stimuli by stimulus intensity. Black bars represent the average pain scores in response to the 7 stimuli at each intensity. Error bars represent the standard error of the mean.

RESULTS

FAST Outcomes

FAST	R^2	ICC	CoV
Mean (SD)	0.453 (0.16)	0.602 (0.16)	0.577 (0.38)
Median	0.49	0.62	0.49
Minimum	0.01	0.08	0.05
Maximum	0.77	0.87	1.56

Table 2. FAST outcomes. Abbreviations: FAST, focused analgesia selection test; SD, standard deviation; ICC, intraclass correlation coefficient; CoV, coefficient of variation.

RESULTS

Interoception Measures

Interoception	Task
Mean (SD)	0.65 (0.23)
Median	0.69
Minimum	0
Maximum	0.98

Table 3. Schandry's task score.

MAIA sub-scales	Mean ± SD	Median	Min-Max
Noticing	3.38 ± 0.9	3.33	0-5
Not Distracting	1.66 ± 0.9	1.50	0-4.5
Not worrying	2.70 ± 1.1	3.0	0.25-5
Attention Regulation	3.02 ± 0.8	3.0	1.14-4.71
Emotional Awareness	3.64 ± 0.8	3.60	1.80-5
Self-Regulation	2.67 ± 0.9	2.57	1-4.43
Trusting	3.81 ± 0.8	4.0	1.67-5
TOTAL	5.44 ± 13.7	2.91	1.88-95

Table 4. Multidimensional Assessment of Interoceptive Awareness questionnaire.

RESULTS

Taste Tasks

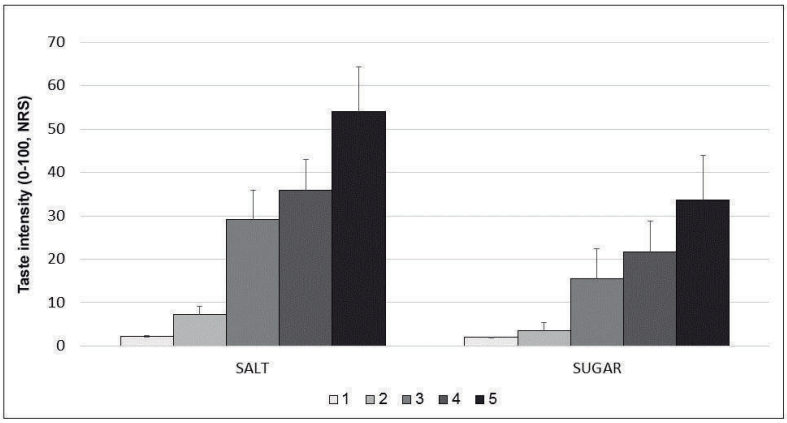


Figure 2. Mean taste scores to taste intensity. Each bar represents the average taste scores in response to the different salt/sugar concentrations. Taste concentrations are labeled 1 to 5, from lowest to highest concentration.

RESULTS

TASTE task Outcomes

SALT	R^2	ICC	CoV
Mean (SD)	0.686 (0.14)	0.831 (0.12)	0.475 (0.21)
Median	0.72	0.86	0.44
Minimum	0.34	0.17	0.12
Maximum	0.92	0.96	0.93

Table 5. Taste task outcomes for salt. Abbreviations: SD, standard deviation; ICC, intraclass correlation coefficient; CoV, coefficient of variation.

SUGAR	R^2	ICC	CoV
Mean (SD)	0.614 (0.18)	0.774 (0.15)	0.496 (0.22)
Median	0.65	0.81	0.47
Minimum	0.03	0.06	0.09
Maximum	0.87	0.96	1.12

Table 6. Taste task outcomes for sugar. Abbreviations: SD, standard deviation; ICC, intraclass correlation coefficient; CoV, coefficient of variation.

Results

ASSOCIATIONS BETWEEN DIFFERENT TASKS

- Positive correlations were found between the salt and sugar reporting accuracy. Subjects with high salt ICC had a high sugar ICC values (Spearman's $r=0.477$, $P<0.001$).

- No significant cross-modal correlations were found (FAST, heartbeat task and taste) ($P>0.05$ for all outcome measures).

- No significant correlations were found between Interoception task and the MAIA questionnaire.

- No significant correlations were found between the different accuracy tasks and the other psychological questionnaires.

DISCUSSION

- The aim of the current study was to investigate if the ability to accuracy report pain is correlated with the ability to accurately report other body sensations:

No associations were found between pain reporting accuracy and reporting accuracy of other sensations.

- Several other studies also did not found correlations between perception of multiple interoception modalities (Vaitl, 1996; Harver et al, 1993; Werner, Duschek, Mattern & Schandry, 2009; Garfinkel et al 2016; Ferentzi et al., 2017; 2018).

DISCUSSION

- Our findings of lack of correlations between interoceptive modalities support the notion that the accuracy is specific for each sensory modality and can't be generalized across modalities or inferred from one modality to another.

- Craig's perspective, suggests that interoception integrates several different sensations from the body running in the same neuronal pathways, describes interoception as general homeostatic function (Craig, 2002; 2009; 2014).

DISCUSSION

- Recently, Smith and Lane (2015):

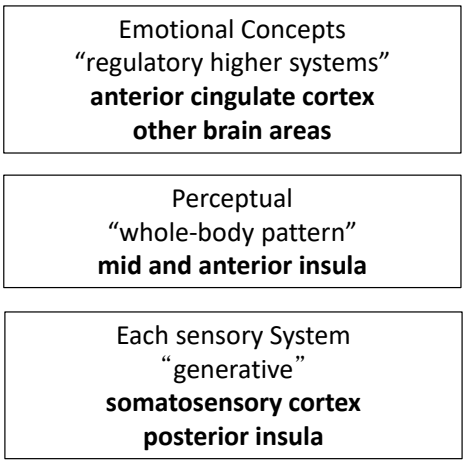


Figura 3 e 4. Model proposed by Smith and Lane (2015) on three hierarchical systems.

CONCLUSION

- The lack of associations between pain reporting accuracy and the accuracy of reporting other sensations, suggests that interoceptive accuracy cannot be generalized to other modalities.

- From a practical point of view, training aimed to improve reporting accuracy of one modality is not predicted to affect the accuracy of reporting sensations of other modalities.

- Knowing that the reporting of bodily signals is essential for emotional processing and for the expression of symptoms it is of the utmost importance to understand how to improve the ability to accurately report body signals.

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PAIN REPORTING ACCURACY DOES NOT CORRELATE WITH ABILITY TO ACCURATELY REPORT OTHER BODILY SENSATIONS

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