Psychosoziale und neurobiologische Determinanten der Inhibition von Schmerzmimik

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Abkürzungsverzeichnis

ACC	Anteriorer cingulärer Kortex
AU	Action Unit
AUs	Action Units
CFCS	Child Facial Coding System
EMG	Elektromyogramm
FACS	Facial Action Coding System
fMRT	Funktionelle Magnetresonanztomographie
mPFC	Medialer Präfrontalkortex
NRS	Numerische Ratingskala
rTMS	Repetitive transkranielle Magnetstimulation
v.a.	vor allem
VAS	Visuelle Analogskala
vgl.	vergleiche
z.B.	zum Beispiel

1. Einleitung

Gesichtsausdrücke sind meist sowohl gut sichtbar als auch gut erkennbar und können deshalb einem aufmerksamen Beobachter viele Informationen über das innere Gefühlsleben, die Gedanken und sogar die Motive des Senders übermitteln (Craig, Prkachin & Grunau, 2011; Ekman, 1999). Daher ist es nicht verwunderlich, dass mimische Reaktionen in zwischenmenschlichen Beziehungen und sozialer Kommunikation eine große Rolle spielen (Darwin, 1872; Halberstadt, Denham & Dunsmore, 2001). Dem mimischen Ausdruck von Schmerz kommt zudem eine besondere Bedeutung zu. Da eine Person meist dann Schmerzen hat, wenn zuvor eine Verletzung aufgetreten ist, ist sie in diesem Moment vulnerabel und auf die Hilfe von Mitmenschen angewiesen, um z.B. medizinisch versorgt zu werden. Die mimische Kommunikation von Schmerz kann neben Empathie auch solches Hilfeverhalten auslösen und somit potentiell das Überleben der Person sichern (Botvinick et al., 2005; Williams, 2002). Der offene Ausdruck der eigenen Schmerzerfahrung über die Mimik muss allerdings nicht notwendigerweise positive Reaktionen nach sich ziehen. So kann es in bestimmten Kontexten (z.B. in Wettkampfsituationen) dazu kommen, dass die durch die Schmerzmimik erkennbare Angreifbarkeit und Verletzlichkeit der betroffenen Person ausgenutzt wird (Craig, 2004, 2009). Demnach scheint es wichtig zu sein, die Intensität bzw. Stärke des mimischen Schmerzausdrucks so zu regulieren, dass die Folgen möglichst förderlich für die eigenen Ziele und Motive ausfallen.

Obwohl allseits anerkannt ist, dass eine solche Regulation des mimischen Schmerzausdrucks stattfindet, ist bisher nur sehr wenig darüber bekannt, wie diese Regulation funktioniert bzw. welche biopsychologischen Mechanismen dieser Regulation zugrunde liegen könnten. Erste Erkenntnisse lieferten fMRT-Befunde, die zeigten, dass die Aktivität fronto-striataler Netzwerke mit der Stärke des mimischen Schmerzausdrucks assoziiert ist (Kunz, Chen, Lautenbacher, Vachon-Presseau & Rainville, 2011). Dabei schienen die beteiligten Areale eine inhibitorische Funktion zu übernehmen, da bei deren Aktivierung eine reduzierte Mimikreaktion auf Schmerzreize zu verzeichnen war. Demnach scheint es möglich, dass die Schmerzmimik darüber reguliert wird, dass Inhibitionsprozesse den mimischen Ausdruck herunterregulieren. Obwohl diese Ergebnisse sehr plausibel erscheinen, bieten sie keinen ausreichenden Beleg dafür, dass Inhibitionsprozesse ausschlaggebend an der Regulation von Schmerzmimik beteiligt sind. Zudem lassen sie nur wenige Schlüsse über die Charakteristika des beteiligten Inhibitionsmechanismus zu.

So ist z.B. unklar, welche Art von Inhibitionsmechanismus für die Regulation von Schmerzmimik besonders relevant ist. Bei Inhibition handelt es sich demnach nicht um ein einheitliches Konstrukt, sondern eher um einen Überbegriff, der unterschiedliche

Mechanismen wie z.B. kognitive und Verhaltensinhibition (Harnishfeger, 1995; Nigg, 2000) umfasst. Obwohl es wahrscheinlich ist, dass Verhaltensinhibition (die Fähigkeit vorherrschende motorische Reaktionen oder Impulse zu kontrollieren bzw. zu inhibieren) am ehesten eine Rolle bei der Regulation von Schmerzmimik spielt, ist in diesem Feld weitere Forschung notwendig.

Die Ergebnisse von Kunz et al. (2011) erlauben ferner keine Aussage darüber, ob die Aktivität der beteiligten Gehirnregionen ausschlaggebend für die Inhibition von Schmerzmimik ist. So bleibt zu klären, welche Rolle die Anteile des identifizierten fronto-striatalen Netzwerks (v.a. der mediale Präfrontalkortex (mPFC)) tatsächlich bei der Inhibition von Schmerzmimik spielen.

Des Weiteren ist bisher unklar, ob und wie die Inhibition des mimischen Schmerzausdrucks durch psychosoziale Faktoren beeinflusst wird. Da die offene Kommunikation von Schmerz abhängig vom Interaktionspartner unterschiedliche Reaktionen hervorrufen kann, scheint es sinnvoll, dass die Inhibition des mimischen Schmerzausdrucks je nach sozialer Situation stärker oder schwächer ausgeprägt ist. Tatsächlich weisen Befunde von anderen Affektzuständen und Studien an Kindern darauf hin, dass die Anwesenheit Fremder die Inhibition steigert (Underwood, Coie & Herbsman, 1992; Vervoort et al., 2008; Yarczower & Daruns, 1982) und es in Anwesenheit Vertrauter zu einer Lockerung der inhibitorischen Kontrolle kommt (Underwood et al., 1992; Vervoort et al., 2011; Wagner & Smith, 1991; Zeman & Garber, 1996). Zum momentanen Zeitpunkt kann allerdings noch keine eindeutige Aussage darüber gemacht werden, wie sich die Anwesenheit unterschiedlich vertrauter Personen auf die Inhibition von Schmerzmimik bei Erwachsenen auswirkt.

Im Rahmen der vorliegenden Dissertation soll nun die Beteiligung von Inhibitionsmechanismen an der Regulation von Schmerzmimik bestätigt werden. Darüber hinaus soll die Inhibition des mimischen Schmerzausdrucks genauer charakterisiert werden, wobei die Erfassung von sowohl psychosozialen als auch neurobiologischen Aspekten einen ganzheitlichen Ansatz gewährleisten soll. Zu diesem Zweck wurden an der Universität Bamberg und dem Universitätsklinikum Erlangen drei Studien durchgeführt, die sich mit folgenden Fragestellungen beschäftigten: (1) Welche Art von Inhibitionsmechanismus ist vorwiegend an der Regulation des mimischen Ausdrucks von Schmerz beteiligt? (2) Ist die Aktivität präfrontaler Areale tatsächlich ausschlaggebend für eine Inhibition des mimischen Schmerzausdrucks? Und (3) ist die Inhibition des mimischen Schmerzausdrucks bei Erwachsenen abhängig vom Interaktionspartner? Im Folgenden wird zunächst eine Einführung in die Thematik gegeben und anschließend erfolgt die Beschreibung der einzelnen Studien. Die Arbeit endet mit einer Zusammenfassung der Ergebnisse und einer übergreifenden Diskussion.

2. Theoretischer Hintergrund

2.1 Der mimische Schmerzausdruck

2.1.1 Bestandteile und Eigenschaften

Neben verbalen Äußerungen und Gestik stellt der mimische Schmerzausdruck einen der wichtigsten und informativsten Kanäle der Schmerzkommunikation dar. Die Information, die aus der Mimik gewonnen wird, kann z.B. dazu verwendet werden verbale Informationen in einen Kontext zu setzen. So gewinnt der verbale Schmerzbericht an Glaubwürdigkeit, wenn er in Kombination mit einem mimischen Schmerzausdruck auftritt (Poole & Craig, 1992). Andererseits kann auch die Schmerzmimik allein den Beobachter über die Empfindungen des Absenders in Kenntnis setzen, ohne dass über Sprache kommuniziert werden muss (Craig et al., 2011; Hadjistavropoulos et al., 2011). Dies setzt allerdings voraus, dass der mimische Schmerzausdruck – wie andere emotionale Gesichtsausdrücke auch – richtig erkannt und gedeutet werden kann. Erste Hinweise darauf stammen aus Untersuchungen, in denen ungeschulte Beobachter Gesichtsausdrücke auf Bildern oder in Videos beurteilen mussten. Dabei zeigte sich, dass diese in der Lage waren Schmerz zu erkennen und den mimischen Schmerzausdruck von anderen emotionalen Gesichtsausdrücken zu differenzieren (Kappesser & Williams, 2002; Simon, Craig, Gosselin, Belin & Rainville, 2008). Beim mimischen Schmerzausdruck scheint es sich demnach um eine spezifische und von anderen mimischen Affektausdrücken abgrenzbare Reaktion zu handeln.

Diese Spezifität zeigt sich auch darin, dass der mimische Schmerzausdruck konstant durch bestimmte Merkmale gekennzeichnet ist. So haben über die Jahre hinweg einige Forschergruppen unabhängig voneinander eine begrenzte Anzahl von mimischen Akten beschrieben, die speziell im Schmerzkontext aufzutreten scheinen. Um die Ergebnisse unterschiedlicher Studien vergleichen zu können, musste dabei eine einheitliche Kodierung mimischer Aktivität verwendet werden. Dies wurde durch die übergreifende Verwendung des Facial Action Coding Systems (kurz FACS; Ekman & Friesen, 1978) realisiert. Beim FACS handelt es sich um ein anatomisch basiertes Kodierschema, das 44 verschiedene Muskelbewegungen der Gesichtsmuskulatur differenziert. Für jede dieser Muskelbewegungen (sogenannte Action Units; kurz AUs) werden Frequenz, Intensität (5-stufige Skala) und Dauer kodiert, so dass die Relevanz unterschiedlicher AUs beurteilt werden kann. Unter Verwendung dieses Schemas ergab sich die folgende Mimikreaktion für schmerzhafte Erfahrungen: Die Kontraktion und das Absenken der Augenbrauen (Musculus corrugator supercilii; AU4), die Kontraktion der Muskulatur um die Augen herum (Musculus orbicularis oculi; AU6/7), das Heben der Oberlippe und die Faltenbildung auf dem Nasenrücken (Musculus levator labii superioris; AU9/10) sowie das

Öffnen des Mundes (Musculus orbicularis oris; AU25/26/27) (z.B. Craig et al., 2011; Kunz, Mylius, Schepelmann & Lautenbacher, 2004, 2008; Prkachin, 1992).

Dieses Set an Muskelbewegungen konnte bei den unterschiedlichsten Schmerzerfahrungen registriert werden. So trat die oben beschriebene Mimikreaktion als Reaktion auf kurze akute Schmerzreize wie z.B. bei Injektionen (Lilley, Craig & Grunau, 1997) und unterschiedlichen experimentellen Schmerzstimulationen auf: Druck (Kunz et al., 2008; Kunz, Scharmann, Hemmeter, Schepelmann & Lautenbacher, 2007; Prkachin, 1992), Hitze (Kunz, Chatelle, Lautenbacher & Rainville, 2008; Kunz et al., 2011), Elektrostimulation (Kunz et al., 2007; Prkachin, 1992) sowie Ischämie und Kälte (Prkachin, 1992). Die gleichen Muskelbewegungen konnten außerdem durch akute Verstärkung klinischer bzw. chronischer Schmerzen ausgelöst werden (z.B. bei chronischem Rückenschmerz (Hadjistavropoulos & Craig, 1994) oder Schulterbeschwerden (Prkachin & Mercer, 1989)). Eine Konstanz weist der Ausdruck zudem über die Altersspanne hinweg auf. Demnach zeigt sich dieser bereits bei Neugeborenen und bleibt auch im Alter erhalten (Hadjistavropoulos et al., 2011; Kunz et al., 2008; Williams, 2002).

Trotz der Vielzahl an konsistenten Befunden ist dieses Set an Muskelbewegungen allerdings keinesfalls als der einzig wahre Schmerzausdruck zu sehen, der so in jeder Schmerzsituation zu beobachten ist. Die beschriebene Kombination an Muskelbewegungen stellt eher eine Art „Kern“ der Schmerzmimik dar, der auch nur in Teilen oder in Kombination mit anderen Muskelbewegungen auftreten kann (Craig et al., 2011; Kunz & Lautenbacher, 2014; Williams, 2002).

2.1.2 Die Rolle und Funktion des mimischen Schmerzausdrucks

2.1.2.1 Abbildungseigenschaften

Neben vielen anderen Funktionen erfüllt der mimische Schmerzausdruck primär die Aufgabe die Schmerzempfindung abzubilden. Dabei scheint der mimische Schmerzausdruck nicht nur darüber Auskunft geben zu können, ob Schmerzen vorhanden sind oder nicht, sondern vermag auch die Stärke des Schmerzes abzubilden. Der Zusammenhang zwischen der Stärke des mimischen Schmerzausdrucks und der berichteten Schmerzstärke scheint allerdings nur dann stark ausgeprägt zu sein, wenn individuelle Unterschiede und motivationale Einflüsse eliminiert werden (Kunz et al., 2004).

Eine weitere Komponente, die scheinbar durch den mimischen Schmerzausdruck enkodiert werden kann, ist die Multi-Dimensionalität von Schmerzerfahrungen. Gemäß der Definition der International Association for the Study of Pain handelt es sich bei Schmerz um *„(…) an unpleasant sensory and emotional experience associated with*

actual or potential tissue damage, or described in terms of such damage". Dementsprechend besteht die Schmerzempfindung zum einen aus einem sensorischen Anteil, der die physikalischen Eigenschaften des Reizes – wie Lokalisation, Dauer und Intensität – abbildet. Zum anderen beinhaltet die Schmerzerfahrung auch ein Gefühl von Unbehagen sowie die emotionale Bewertung des Schmerzreizes, was als affektiv-emotionale Komponente bezeichnet wird. Im Schmerzausdruck scheinen diese Anteile ebenfalls einzeln vertreten zu sein (Kunz, Lautenbacher, LeBlanc & Rainville, 2012). So wird eine erhöhte Schmerzsensorik von einer verstärkten Schutzreaktion des Auges (verstärkte Kontraktion der Muskulatur um die Augen herum (AU6/7); Craig et al., 2011) begleitet. Ein erhöhter Schmerzaffekt hingegen führte zu einem vermehrten Auftreten von Muskelbewegungen, die allgemein bei negativem Affekt zu beobachten sind (Kontraktion der Augenbrauen (AU4) und des Levator-Muskels (AU9/10)).

2.1.2.2 Kommunikative Funktionen des mimischen Schmerzausdrucks

Über die reine Abbildung der Schmerzempfindung hinaus erfüllt die Schmerzmimik im Rahmen von Kommunikation weitere Funktionen. Dabei hängt die jeweilige Funktion immer von der Kommunikationsform ab, die der mimische Schmerzausdruck darstellt. Laut Hadjistavropoulos et al. (2011) lässt sich jede Form von Schmerzkommunikation einer von drei Kategorien zuordnen; nämlich „action", „interaction" und „transaction".

„Action" bezieht sich dabei auf die individuelle Neigung bzw. den inneren Antrieb Schmerz offen zu kommunizieren; d.h. damit sind eher automatisierte Handlungen gemeint. So stellt der mimische Schmerzausdruck als „action" so etwas wie eine Erscheinungsform der Schmerzerfahrung dar, hinter der nicht unbedingt eine Kommunikationsabsicht stehen muss (Craig, 2009; Craig et al., 2011; Hadjistavropoulos et al., 2011). Bereits diese Form von Kommunikation ist allerdings funktionell, da das automatisch generierte Signal anderen als Warnung vor physischen Bedrohungen und Gefahr dienen kann (Williams, 2002).

Bei „interaction" und „transaction" kommt es nun zu einem intendierten gegenseitigen Austausch von Informationen zwischen zwei Personen und der Beobachter des mimischen Schmerzausdrucks soll in die Lage versetzt werden die Ziele, Gefühle und Gedanken des Senders zu verstehen. In diesem Fall können automatisierte Mimikreaktionen auf schmerzhafte Erfahrungen auch „überschrieben", d.h. durch willentliche Kontrolle verstärkt, reduziert oder abgewandelt werden (Craig et al., 2011; Rinn, 1984). Die Besonderheit der „transaction" liegt darin, dass nicht nur eine dyadische Kommunikation stattfindet, sondern dass diese auch ein Ergebnis zur Folge hat. So kann das Dekodieren einer mimischen Schmerzbotschaft den Empfänger z.B. dazu veranlassen der Person mit Schmerzen zu helfen oder ihr gar eine medizinische

Behandlung zukommen zu lassen (Williams, 2002). Dementsprechend kann die mimische Kommunikation von Schmerz sogar dazu beitragen, das Überleben einer Person zu sichern, was sicherlich zu einer ihrer wichtigsten Funktionen zählt. Das Ergebnis einer „transaction“ muss allerdings nicht notwendigerweise positiv für den Sender der mimischen Schmerzbotschaft ausfallen. Neben altruistischen Verhaltensweisen können demnach auch negative Reaktionen ausgelöst werden. Dazu zählt, dass die Angreifbarkeit und Verletzlichkeit der Person mit Schmerzen ausgenutzt werden könnte, aber auch – abhängig vom Empfänger und der jeweiligen Situation – dass es zur Bestrafung der offenen Zurschaustellung von Schmerz kommt (Craig, 2004, 2009).

Zusammenfassend lässt sich also festhalten, dass dem mimischen Schmerzausdruck unterschiedliche Funktionen zukommen, je nachdem welche Form von Kommunikation er darstellt. Außerdem unterscheidet sich je nach Kommunikationsform das Ausmaß der aktiven Modulierbarkeit des Ausdrucks.

2.2 Mimisches „Gating“

2.2.1 Inhibition als potentieller Kontrollmechanismus von Schmerzmimik

Wie im vorausgehenden Abschnitt angedeutet, kann die offene mimische Kommunikation von Schmerzen unterschiedliche Folgen haben. Dementsprechend scheint es essentiell, dass das vorwiegend automatisch generierte Signal (Blair, 2003; Darwin, 1872) reguliert und nicht vollkommen unkontrolliert nach außen getragen wird. Bisher ist jedoch nur sehr wenig darüber bekannt, welche Mechanismen an einer solchen „Ausgangskontrolle“ des mimischen Schmerzausdrucks beteiligt sind und somit (mit-)bestimmen, wieviel der generierten Mimikreaktion tatsächlich zur Schau gestellt wird.

Erste Hinweise auf einen möglichen Regulationsmechanismus lieferten die Ergebnisse einer kürzlich durchgeführten fMRT-Studie (Kunz et al., 2011). Hier zeigte sich, dass die Stärke des mimischen Schmerzausdrucks bei experimenteller Hitzeschmerz-Stimulation mit der Aktivität fronto-striataler Netzwerke in Verbindung stand. Genauer gesagt, drückten die Probanden ihren Schmerz umso weniger über die Mimik aus, je höher die Aktivität des medialen Präfrontalkortex (mPFC) sowie des Nucleus Caudatus war. Dieser Zusammenhang zeigte sich zum einen darin, dass diese fronto-striatale Aktivität bei weniger expressiven Probanden stärker ausgeprägt war. Zum anderen konnte auch bei Innersubjektvergleichen festgestellt werden, dass Durchgänge, in denen kein mimischer Schmerzausdruck auftrat, mit einer höheren Aktivität von mPFC und Nucleus Caudatus einhergingen. Aus früheren Studien war bereits bekannt, dass fronto-striatale Areale an motorischer Inhibition beteiligt sind (Aron et al., 2007; Ridderinkhof, van den Wildenberg, Segalowitz & Carter, 2004). Der Befund einer erhöhten Aktivierung dieser Areale bei

einem reduzierten mimischen Schmerzausdruck deutet nun darauf hin, dass Inhibitionsprozesse auch bei der Regulation von Schmerzmimik eine Rolle spielen könnten. Es scheint demnach plausibel, dass fronto-striatale Inhibitionsmechanismen den mimischen Schmerzausdruck herab regulieren.

Diese Ergebnisse stehen im Einklang mit einer früheren Studie, die sich mit der Gehirnaktivierung während des mimischen Ausdrucks von Ekel befasste. In dieser Studie wurden die Probanden dazu instruiert den mimischen Ausdruck von Ekel zu inhibieren, was ebenfalls mit einer erhöhten präfrontalen Aktivität einherging (Goldin, McRae, Ramel & Gross, 2008). Dass auch in diesem Fall eine präfrontale Aktivierung mit einer Reduktion des mimischen Ausdrucks verbunden war, deutet wiederum darauf hin, dass präfrontale Areale bei der Inhibition von Mimikreaktionen eine besonders große Rolle spielen. Im Schmerzkontext scheint dabei speziell der mediale Teil des präfrontalen Kortex relevant zu sein. Die bisherigen Ergebnisse lassen allerdings keine Aussage darüber zu, ob die Aktivierung präfrontaler Areale ausschlaggebend dafür ist, dass es zur Inhibition von Schmerzmimik kommt. So muss das gemeinsame Auftreten von reduzierter Schmerzmimik und erhöhter mPFC-Aktivität nicht unbedingt auf einen kausalen Zusammenhang hindeuten. Es ist auch möglich, dass ein dritter Prozess, der z.B. an der Schmerzverarbeitung selbst beteiligt ist, die beiden Effekte vermittelt.

Obwohl sie nur erste Hinweise liefern, bilden die Befunde und Interpretationen von Kunz et al. (2011) die Grundlage für eine erste Hypothese zur Regulation von Schmerzmimik. Da sie annehmen ließen, dass Inhibitionsmechanismen daran beteiligt sind, die Schmerzmimik zu regulieren, sollen in der vorliegenden Arbeit Veränderungen in der Stärke des mimischen Schmerzausdrucks unter Inhibitionsperspektive betrachtet werden. Auf diese Weise soll geklärt werden, welche Relevanz die Inhibition von Schmerzmimik hat und wie diese genau beschaffen ist.

2.2.2 Arten von Inhibition

Bei einer solchen Überlegung muss beachtet werden, dass es sich bei Inhibition nicht um ein einheitliches Konstrukt handelt, sondern dass unterschiedliche Prozesse in diese Kategorie fallen. Um den an der Schmerzmimikregulation beteiligten Mechanismus genau definieren zu können, muss also auch herausgefunden werden, welche Art von Inhibition dafür besonders relevant ist. Eine grobe Unterteilung wird in der Inhibitionsliteratur üblicherweise zwischen „kognitiver“ und „Verhaltensinhibition“ vorgenommen (Harnishfeger, 1995; Nigg, 2000). Während „kognitive Inhibition“ den Vorgang des Kontrollierens mentaler Prozesse, wie Gedächtnis oder Aufmerksamkeit, bezeichnet, bezieht sich „Verhaltensinhibition“ eher auf die Fähigkeit vorherrschende motorische Reaktionen oder Impulse zu kontrollieren bzw. zu inhibieren. Da es sich bei der Mimik um

eine motorische Reaktion handelt (Craig et al., 2011), scheint „Verhaltensinhibition“ gemäß dieser Definition am relevantesten für die Regulation des mimischen Schmerzausdrucks zu sein. Diese Vermutung gilt es allerdings noch mit Befunden zu untermauern.

2.2.3 Entwicklung mimischer Inhibition

Dass Inhibitionsmechanismen per se bei der Regulation des mimischen Schmerzausdrucks eine wichtige Rolle spielen könnten, kann auch aus Beobachtungen bezüglich der Entwicklung mimischen Ausdrucksverhaltens abgeleitet werden. Ein „Grundkonzept“ der Mimik scheint zunächst angeboren zu sein. Dementsprechend sind bereits Neugeborene dazu in der Lage, bestimmten Affektzuständen, u.a. auch Schmerz, über ihre Mimik Ausdruck zu verleihen (Craig et al., 2011; Ekman, 1999; Grunau & Craig, 1987; Johnston, Stevens, Craig & Grunau, 1993). In dieser frühen Lebensphase gelten Mimikreaktionen allerdings eher als reflexiv und unkontrolliert (Craig et al., 2011). Erst im Laufe der Sozialisation entwickelt sich allmählich die Fähigkeit die Stärke des mimischen Ausdrucks an die Anforderungen einer bestimmten Situation anzupassen und somit eine selektive Kontrolle über die Mimik auszuüben (Craig, Versloot, Goubert, Vervoort & Crombez, 2010; Izard, 1971). Speziell beim Ausdruck negativer Affektzustände geht diese über die Sozialisation erworbene Kontrolle hauptsächlich mit einer Reduktion des mimischen Ausdrucks einher (Izard, 1971). Dies spricht wiederum dafür, dass tatsächlich eine aktive Inhibition von Mimik erlernt wird. Die offenkundige Zurschaustellung der eigenen Emotionen über die Mimik scheint demnach die „Voreinstellung“ zu sein, mit der man geboren wird. Im Zuge der sozialen Entwicklung scheint man dann zu lernen diese „Voreinstellung“ zu inhibieren.

Folgt man dieser Argumentation sollten sich, abhängig von der individuellen Lerngeschichte, unterschiedliche Ausprägungen an mimischer Inhibition ergeben. Tatsächlich finden sich grundlegende individuelle Unterschiede in der mimischen Expressivität von Schmerz. So kommunizieren verschiedene Personen ihren Schmerz unterschiedlich stark über die Mimik, unabhängig davon wie intensiv der Schmerz erlebt und berichtet wird. Es zeigt sich daher – ähnlich wie bei anderen Affektzuständen (vgl. Gross & Levenson, 1993; Richards & Gross, 2000) – eine große Bandbreite mimischer Expressivität. Diese reicht von starker mimischer Expressivität bis hin zu Stoizismus, bei dem so gut wie keine Mimik gezeigt wird; und das selbst bei starken Schmerzen.

2.2.4 Soziale Vertrautheit als Einflussfaktor auf die Inhibition von Schmerzmimik

Unabhängig von diesen generellen individuellen Unterschieden in der mimischen Schmerzexpressivität scheint es Situationen zu geben, die die Inhibition von mimischen

Reaktionen begünstigen bzw. reduzieren. Bei anderen Affektzuständen ist bereits gut dokumentiert, wie unterschiedliche Interaktionspartner die Inhibition des mimischen Ausdrucks beeinflussen. So zeigen verschiedene Studien, dass der mimische Ausdruck von sowohl Freude (Yarczower & Daruns, 1982) als auch von negativen Emotionen wie z.B. Wut (Underwood et al., 1992) in einer formalen Situation (z.B. mit einem Lehrer oder einem Versuchsleiter) reduziert wird. In Anwesenheit eines Vertrauten, wie z.B. einem Freund oder den Eltern, zeigten Probanden hingegen positive (Freude: Wagner & Smith, 1991) wie auch negative Emotionen (Trauer, Wut, Schmerz: Underwood et al., 1992; Wagner & Smith, 1991; Zeman & Garber, 1996) in einem stärkeren Ausmaß. Die Grundlage dieser sozialen Modulation mimischer Reaktionen wird in sogenannten „social display rules“ vermutet. Diese sozialen Regeln werden ebenfalls im Lauf der Entwicklung gelernt und geben an, ob und in welchem Ausmaß eine mimische Reaktion in einer bestimmten Situation kulturell angemessen ist (Brody & Fischer, 2000; Davis, 1995; Saarni, 1984; Underwood et al., 1992). Das Erlernen dieser Regeln scheint demnach im Bewusstsein zu verankern, dass eine offene Zurschaustellung von Emotionen in formalen Situationen unangemessen ist und daher inhibiert werden muss, Emotionen aber gegenüber Vertrauten frei kommuniziert werden dürfen.

Bei der Betrachtung dieser Ergebnisse sollte nicht unerwähnt bleiben, dass die berichteten Studien trotz konsistenter Befunde einige methodische Mängel aufweisen. So stützen sich die meisten Ergebnisse nur auf Beobachterurteile (Wagner & Smith, 1991; Yarczower & Daruns, 1982) oder den Selbstbericht der Probanden bezüglich der Regulation des mimischen Ausdrucks (Underwood et al., 1992; Zeman & Garber, 1996). Problematisch ist dabei, dass der Selbstbericht oft nur mittelmäßig mit der tatsächlichen Regulation korreliert (Gross & John, 1997), da diese nicht unbedingt bewusster Reflexion zugänglich sein muss.

Im Schmerzkontext existieren ebenfalls Hinweise darauf, dass die Stärke mimischer Inhibition auf den jeweiligen Interaktionspartner angepasst wird. So zeigten Studien bei Kindern, dass diese – im Vergleich zu einer Situation, in der sie alleine waren – ihren Eltern gegenüber Schmerzen mimisch freier kommunizierten und den mimischen Schmerzausdruck in Anwesenheit eines Fremden reduzierten (Vervoort et al., 2008; Vervoort et al., 2011). Die raren Befunde bei Erwachsenen zeichnen ein ähnliches Bild, wenngleich sich diese bisher nur auf Beobachterurteile (Kleck et al., 1976) und Untersuchungen (Vlaeyen et al., 2009) mit dem Child Facial Coding System (CFCS; Chambers, McGrath, Gilbert & Craig, 1996) stützen. In Anwesenheit eines Fremden reduzierten demnach auch Erwachsene den mimischen Schmerzausdruck (Kleck et al., 1976; Vlaeyen et al., 2009). Insgesamt lässt die Befundlage im Schmerzkontext somit vermuten, dass auch hier die Stärke mimischer Inhibition auf den Interaktionspartner

angepasst wird. Bisher sind allerdings keine eindeutigen Aussagen möglich, da es an systematischen, FACS-basierten Untersuchungen an erwachsenen Probanden mangelt. Ferner wurde bisher nicht untersucht, wie sich die Inhibition des mimischen Ausdrucks bei Erwachsenen in Anwesenheit einer vertrauten Person verhält.

2.3 Übergeordnete offene Fragestellungen und Zielsetzung der eigenen Forschung

Die oben dargestellten Befunde zeigen auf, dass in den letzten Jahren viele Erkenntnisse bezüglich der Regulation des mimischen Schmerzausdrucks gewonnen wurden und eine begründete Annahme besteht, dass Inhibitionsmechanismen in diesem Kontext eine wichtige Rolle spielen. Trotzdem bleiben viele entscheidende Fragen bezüglich dieses Regulationsmechanismus bisher unbeantwortet und die Befundlage ist nicht ausreichend, um die Relevanz von Inhibition für die Regulation von Schmerzmimik genau einordnen zu können. Daher sollen in der vorliegenden Arbeit unterschiedliche Facetten der Inhibition des mimischen Schmerzausdrucks genauer untersucht werden, um die Grundlagen dieses Mechanismus und dessen Bedeutsamkeit besser verstehen zu können.

Zu diesem Zweck soll in einer ersten Studie zunächst die Beteiligung von Inhibitionsmechanismen an der Regulation von Schmerzmimik bestätigt werden. Darüber hinaus soll in dieser Studie (I) der Inhibitionsmechanismus identifiziert werden, der dabei die entscheidende Rolle spielt.

Zur weiteren neurobiologischen Charakterisierung des Mechanismus soll durch eine nicht-invasive Aktivitätsreduktion des medialen Präfrontalkortex (mittels repetitiver transkranieller Magnetstimulation (rTMS)) untersucht werden, ob präfrontale Aktivität – wie von der Literatur angedeutet – tatsächlich ausschlaggebend für die Inhibition des mimischen Schmerzausdrucks ist (Studie II).

Die vorliegende Arbeit soll zudem erfassen, inwieweit die Inhibition des mimischen Schmerzausdrucks bestimmten psychosozialen Einflüssen unterliegt (Studie III). Dabei soll explizit erfasst werden, wie sich die Anwesenheit unterschiedlich vertrauter Interaktionspartner bei Erwachsenen auf die Inhibition von Schmerzmimik auswirkt.

3. Eigene experimentelle Arbeiten

Unter der Leitung von PD Dr. Miriam Kunz und Prof. Dr. Stefan Lautenbacher erfolgten an der Universität Bamberg und dem Universitätsklinikum Erlangen drei Studien, mithilfe derer die Inhibition des mimischen Ausdrucks bei Schmerz genauer untersucht werden sollte. Studie I und II beschäftigten sich mit der Identifikation des spezifischen biopsychologischen Inhibitionsmechanismus unter Berücksichtigung der daran beteiligten Gehirnareale. In Studie III wurde erfasst, welchen Einfluss die Vertrautheit der Interaktionspartner auf die Inhibition von Schmerzmimik hat.

Trotz der inhaltlichen Unterschiede, ergaben sich in der methodischen Umsetzung der drei Fragestellungen einige Gemeinsamkeiten. Um Redundanzen in den später folgenden Studienbeschreibungen zu vermeiden, werden diese Gemeinsamkeiten im folgenden Abschnitt vorgestellt.

3.1 Gemeinsamkeiten in der Methodik

3.1.1 Phasische Schmerzstimulation

In allen drei Studien wurde die mimische Aktivität während phasischer Schmerzstimulation aufgezeichnet. In den Studien I und III erfolgte die Applikation von schmerzhaften sowie nicht-schmerzhaften Hitzereizen an der linken Wade über eine 3 x 3 cm² Kontaktthermode (Medoc TSA 2001; Medoc Ltd, Ramat Yishai, Israel). Die applizierten Reize wurden jeweils auf die individuelle Schmerzschwelle angepasst (-1°C, +3°C), welche zuvor mittels Herstellungsmethode ermittelt wurde. Dabei sollten die Probanden selbst – ausgehend von einer Temperatur von 35°C – die Temperatur einstellen, bei der sie beginnenden Schmerz verspürten (zwei Übungsdurchgänge, vier Testdurchgänge). Bei der Stimulation (schmerzhaft/nicht-schmerzhaft) stieg die Temperatur von einer Baseline-Temperatur von 38°C jeweils auf das Zielniveau an (rate of rise: 4°C/Sekunde), welches dann für 5 s appliziert wurde. In einem Stimulationsblock erfolgte die randomisierte Applikation von zehn schmerzhaften sowie zehn nicht-schmerzhaften Reizen.

In Studie II fiel die Wahl auf eine standardisierte Druck- und Hitzestimulation. Schmerzhafte sowie nicht-schmerzhafte Druckreize wurden mithilfe eines Druckalgometers (Algometer Typ II, Somadic Sales AB, Hörby, Sweden; Auflagefläche = 1 cm² Durchmesser) an der Innenseite des Unterarms und an der Schulter (Trapezmuskel) verabreicht. Es erfolgte die Präsentation von vier schmerzhaften (500 kPa) und vier nicht-schmerzhaften Reizen (200 kPa) in randomisierter Reihenfolge, wobei die Druckstimulation jeweils 5 s andauerte. Zusätzlich erfolgte eine Heißwasserstimulation, bei der die Probanden ihre Hand mehrmals in ein Wasserbad

(Witeg GmbH, WiseCircu WCB-22, Wertheim) mit schmerzhafter (47,5°C) Temperatur tauchen sollten. Zwischen den Reizen wurde die Hand in ein Wasserbad mit einer Temperatur von 35°C (Baseline) getaucht. Insgesamt wurden auf diese Art sechs schmerzhafte Hitzereize verabreicht, die jeweils mindestens 10 s lang waren. Die Stimulation erfolgte für beide Reizarten sowohl auf der rechten, als auch auf der linken Körperseite.

3.1.2 Mimikanalyse mittels Facial Action Coding System (FACS)

Während der Schmerzstimulation wurde das Gesicht der Probanden gefilmt, wobei eine – für die Probanden nicht sichtbare – LED-Lampe den Startpunkt und die Dauer der einzelnen Reize anzeigte. Mithilfe des Facial Action Coding Systems (Ekman & Friesen, 1978) erfolgte offline die Kodierung der mimischen Aktivität in diesen Video-Aufnahmen. Dies führten zertifizierte FACS-Kodierer oder von diesen trainierte Personen durch. Die Interraterreliabilität (berechnet mithilfe der Ekman-Friesen-Formel (Ekman & Friesen, 1978)) lag dabei immer zwischen 0,82 und 0,87. Die FACS-Kodierung erfolgte bei jedem Reiz über die Zeitspanne hinweg, in der die Zielintensität erreicht war (5 s/10 s), inklusive 2 s nach Stimulus-Ende, da die Mimikreaktion oftmals noch nach Beendigung des Reizes anhält. Diese Kodierung erfolgte sowohl für die schmerzhaften als auch für die nicht-schmerzhaften Reize. Zum Zweck notwendiger Datenreduktion wurden bestimmte mimische Reaktionen zusammengefasst (AU1/2, AU6/7, AU9/10 and AU25/26/27). Dies erfolgte bereits in vielen anderen Studien, ohne dass ein Informationsverlust eintrat (z.B. Kunz et al., 2004; Kunz et al., 2007; Prkachin, 1992).

Schmerzrelevante AUs wurden basierend auf früheren Studien (z.B. Kunz et al., 2008; Kunz et al., 2007) folgendermaßen ausgewählt: (1) Die AUs mussten in mehr als 5% der aufgezeichneten schmerzhaften Durchgänge auftreten und (2) häufiger in schmerzhaften als in nicht-schmerzhaften Durchgängen vorkommen (Effektgröße $d \geq 0,5$). Die Kriterien für die Auswahl schmerzrelevanter AUs bei der Hitze-Stimulation in Studie II waren aufgrund längerer Stimulationszeiten und dem Fehlen nicht-schmerzhafter Reize (anstelle galt 35°C als Baseline-Referenzkategorie) leicht verändert: (1) Die AUs mussten demnach in mehr als 10% der aufgezeichneten schmerzhaften Durchgänge auftreten und (2) häufiger in schmerzhaften als in Baseline-Durchgängen vorkommen (Effektgröße $d \geq 0,5$).

In allen Studien wurde im nächsten Schritt die mittlere Frequenz und Intensität der so ausgewählten AUs für jede AU einzeln multipliziert. Anschließend wurden diese Produkte über alle ausgewählten AUs hinweg gemittelt, woraus ein sogenannter *composite score* schmerzrelevanter mimischer Aktivität entstand. Da diese Werte meist keiner Normalverteilung folgen, erfolgte in einem letzten Schritt eine *square root* Transformation der *composite scores*.

3.2 Studie I

Karmann, A. J., Lautenbacher, S., Kunz, M. (2015). The role of inhibitory mechanisms in the regulation of facial expressiveness during pain. *Biological Psychology 104,* S. 82 - 89.

3.2.1 Theoretischer Hintergrund

Trotz erster Hinweise darauf, dass Inhibitionsmechanismen an der Regulation von Schmerzmimik beteiligt sind, bedarf es weiterer Forschung, um dies als zuverlässige Schlussfolgerung zu sehen. In Studie I sollte deshalb der Zusammenhang zwischen unterschiedlichen Inhibitionsmaßen und der Stärke des mimischen Schmerzausdrucks untersucht werden. Sollte die Regulation von Schmerzmimik tatsächlich stark von Inhibitionsmechanismen beeinflusst werden, ist davon auszugehen, dass sich ein Zusammenhang zwischen der Stärke des mimischen Schmerzausdrucks und anderen Indikatoren von Inhibition ergibt.

Ferner ist bisher unklar, welche Art von Inhibitionsmechanismus für die Regulation von Schmerzmimik ausschlaggebend sein könnte. Wie in 2.2.2 beschrieben wird üblicherweise zwischen „kognitiver“ und „Verhaltensinhibition“ unterschieden (Harnishfeger, 1995; Nigg, 2000), wobei „Verhaltensinhibition“ für die Regulation des mimischen Schmerzausdrucks am ehesten als relevant erscheint. Um einen möglichst großen Anteil des Spektrums „Verhaltensinhibition“ abzudecken, erfolgte daher in Studie I die Erhebung unterschiedlicher Inhibitionsmaße. Dabei erfolgte die Wahl der Maße so, dass unterschiedliche Mechanismen erfasst wurden, die aus theoretischer Sicht stärker und weniger stark mit der Regulation von Schmerzmimik in Verbindung stehen. So wurde zunächst ein Eyetracking-Paradigma durchgeführt, bei dem die Inhibition von Sakkaden zu plötzlich auftauchenden, peripheren Stimuli gemessen wurde (Antisakkaden-Aufgabe; Hallett, 1978). Mithilfe dieser Aufgabe wurde demnach erfasst, wie gut eine Reaktion inhibiert werden kann, die der Mimik sehr ähnlich ist (okulomotorische Inhibition von automatischen Orientierungsreaktionen bzw. Reflexen). Als zweites, theoretisch etwas weiter entferntes Maß wurde der Stroop-Test (Stroop, 1935) durchgeführt, bei dem die Farbe bzw. Bedeutung von dargebotenen Farbwörtern benannt werden sollte. Obwohl bei dieser Aufgabe motorische Inhibition ebenfalls eine Rolle spielt, erfordert die Bearbeitung zusätzlich höhere kognitive Prozesse wie das Dekodieren von Wortmaterial (Nigg, 2000). Um „Verhaltensinhibition“ auf Ebene von Persönlichkeitsvariablen zu erheben und dies als drittes, am weitesten entferntes Maß einzuführen, erfolgte zudem die Aufnahme der Impulsive Behavior Scale (UPPS; Whiteside & Lynam, 2001) in Studie I. Diese erfasst vier Dimensionen impulsiven Verhaltens und wurde bereits mit unterschiedlichen Inhibitionsmechanismen in Verbindung gebracht (Gay, Rochat, Billieux, d’Acremont & van der Linden, 2008; Roberts, Fillmore & Milich, 2011).

Zusammenfassend war das Ziel von Studie I die Beteiligung von Inhibitionsmechanismen an der Regulation von Schmerzmimik zu bestätigen und herauszufinden, welche Art von Inhibitionsmechanismus dafür besonders ausschlaggebend ist. Zu diesem Zweck wurde der Zusammenhang zwischen der Stärke des mimischen Schmerzausdrucks und unterschiedlichen Inhibitionsmaßen (Antisakkaden-Aufgabe, Stroop, UPPS) erfasst. Bisherige Befunde ließen davon ausgehen, dass sich dabei ein negativer Zusammenhang ergeben sollte, da der mimische Schmerzausdruck umso geringer ausfallen sollte, je mehr Inhibition ausgeübt wird. Dieser negative Zusammenhang sollte mit der theoretisch verwandten Antisakkaden-Aufgabe (Indikator motorischer Inhibition) wesentlich ausgeprägter sein, als mit den theoretisch weiter entfernten Maßen des Stroop-Tests (Indikator von kognitiver und Verhaltensinhibition) und des UPPS (selbst-berichtete Impulskontrolle).

3.2.2 Methode

An Studie I nahmen 49 junge, gesunde Erwachsene (24 Frauen; Alter: M = 22,2; SD = 3,1 Jahre) teil. Das Experiment war in zwei Blöcke untergliedert. Im ersten Block erfolgt die Messung mimischer Reaktionen auf die bereits beschriebene phasische Hitzestimulation (Kontaktthermode). Nach jedem Reiz gaben die Probanden die subjektiv empfundene Schmerzintensität mithilfe einer visuellen Analogskala (VAS; 100 mm) an. Dabei entsprach das linke Ende der Skala „keiner Empfindung“, die Mitte „beginnendem Schmerz“ und das rechte Ende „extrem starkem Schmerz“, so dass jeweils die Hälfte der Skala zur Bewertung schmerzhafter bzw. nicht-schmerzhafter Reize verwendet werden konnte. Um eine höhere Auflösung der Messung zu gewährleisten, erfolgte in diesem Experiment – zusätzlich zur FACS-Kodierung der Mimik bei allen Reizen – die Ableitung eines Elektromyogramms (EMG) vom Musculus orbicularis oculi. Zu diesem Zweck wurden zwei mit Elektrodengel gefüllte Ag/AgCl Elektroden unter dem linken Auge angebracht (gemäß der Platzierungsempfehlungen von Fridlund & Cacioppo, 1986). Die Aufzeichnung der Rohsignale erfolgte mithilfe des Gerätes SIGMA Plpro/Type Databox DB 36. Mit dem Programm „Vision Analyzer“ wurden die Signale dann offline gefiltert, gleichgerichtet und integriert. Im Anschluss erfolgte die Bildung von Summenwerten für die 7 s nach Stimulus-Onset, um Werte zu schaffen, die mit dem FACS vergleichbar waren.

Im zweiten Block des Experiments wurden unterschiedliche Inhibitionsmaße erhoben. Dies wurde zum einen mithilfe der Antisakkaden-Aufgabe (Hallett, 1978) umgesetzt. In diesem Eyetracking-Paradigma sollten die Probanden einen plötzlich auftauchenden Stimulus entweder mit dem Blick verfolgen (Prosakkaden-Bedingung) oder sich von diesem abwenden (Antisakkaden-Bedingung). Relevante Größen stellten dabei die

Latenz der 1. richtigen Sakkade (hin zum Reiz in der Prosakkaden-Bedingung und weg vom Reiz in der Antisakkaden-Bedingung) und der prozentuale Anteil inkorrekter Sakkaden dar. Als Maß der Inhibitionsfähigkeit wurde für beide Größen der gemittelte Wert der Prosakkaden-Durchgänge vom gemittelten Wert der Antisakkaden-Durchgänge abgezogen. Der Stroop-Test (Stroop, 1935) wurde nachfolgend als zweites, theoretisch etwas weiter entferntes Inhibitionsmaß durchgeführt. Dabei sollten die Probanden in den vier Bedingungen (Farbbenennung nicht semantischer Stimuli – CN_{neu}; Farbbenennung inkongruent gefärbter Farbwörter – CN_{incg}; Lesen schwarz gefärbter Farbwörter – WN_{neu}; Lesen inkongruent gefärbter Farbwörter – WN_{incg}) mithilfe von vier farbkodierten Tasten so schnell und so richtig wie möglich reagieren. Als Maß der Inhibitionsfähigkeit dienten der *Stroop-Effekt* ($CN_{incg.}$ – CN_{neu}) und der *Reverse Stroop-Effekt* (WN_{incg} – WN_{neu}). Für beide Inhibitionsmaße (Antisakkaden-Aufgabe/Stroop) ergab sich demnach folgender Grundsatz: Je höher der Wert, desto geringer die Inhibitionsfähigkeit. Zuletzt füllten die Probanden noch die deutsche Version der Impulsive Behaviour Scale (UPPS; Whiteside & Lynam, 2001) aus.

3.2.3 Ergebnisse

Regressionsanalysen ergaben, dass die Variablen des UPPS nicht signifikant dazu beitragen konnten die Stärke des mimischen Schmerzausdrucks vorherzusagen. Dies galt sowohl wenn die FACS-Kodierung als auch wenn das EMG des M. orbicularis oculi als Maß der Schmerzmimik – und somit auch als Kriterium – verwendet wurde. Ebenso wenig konnte in beiden Fällen (FACS, EMG) die Hinzunahme der Stroop Variablen im zweiten Schritt eine erhöhte Vorhersagekraft des Modells bewirken. Demnach schien die Stärke des mimischen Schmerzausdrucks von solchen Inhibitionsmechanismen unabhängig zu sein, die durch den UPPS oder den Stroop erfasst werden. Erst die Hinzunahme der Variablen der Antisakkaden-Aufgabe im letzten Block erhöhte signifikant die Vorhersagekraft des Modells. Dies war sowohl für FACS als auch für EMG als Maß der Schmerzmimik nachzuweisen. Die Regulation des mimischen Schmerzausdrucks stand demnach mit dem in der Antisakkaden-Aufgabe erfassten Inhibitionsmechanismus in Zusammenhang. Dieser Zusammenhang war negativ ausgeprägt, was sich darin zeigte, dass die Probanden ihren Schmerz desto stärker über die Mimik zeigten, je geringer die Inhibition in der Antisakkaden-Aufgabe ausgeprägt war.

3.2.4 Diskussion

Wie erwartet, zeigte sich ein starker negativer Zusammenhang zwischen der Fähigkeit automatische, motorische Reaktionen zu inhibieren (erfasst durch die Antisakkaden-Aufgabe) und der mimischen Aktivität bei schmerzhafter Stimulation. Je stärker die inhibitorische Kontrolle okulomotorischer Reaktionen ausgeprägt war, desto weniger stark

zeigten die Probanden ihren Schmerz über die Mimik. Dieser Zusammenhang erwies sich als sehr robust, da er unabhängig davon festzustellen war, ob FACS oder EMG als Maß der mimischen Aktivität verwendet wurden. Gemeinsam mit den berichteten Befunden aus Bildgebungsstudien (Goldin et al., 2008; Kunz et al., 2011) unterstützen diese Ergebnisse demnach die Interpretation, dass Inhibitionsmechanismen eine wichtige Rolle bei der (Herunter-)Regulation von Schmerzmimik spielen.

Dass dieser Schluss allerdings nicht für alle Arten von Inhibition zulässig ist, zeigt die Divergenz der Effekte der Antisakkaden-Aufgabe und des Stroop-Tests. So konnte die Stärke des mimischen Schmerzausdrucks nur durch die Leistung in der Antisakkaden-Aufgabe, aber nicht durch die Leistung im Stroop-Test vorhergesagt werden. Eine genauere Betrachtung der beiden Aufgaben macht deutlich warum dies der Fall sein könnte. Während die Antisakkaden-Aufgabe die Fähigkeit misst, eine reflexive Sakkade zu unterdrücken (Hutton & Ettinger, 2006), erfordert der Stroop-Test die Inhibition einer eher kognitiven Reaktion, die auf semantischer Verarbeitung basiert (Nigg, 2000). Obwohl Mimikreaktionen auch willkürlich gesteuert sein können, sind mimische Reaktionen auf experimentelle Schmerzreize, die in einem Laborkontext (mit so gut wie keinen sozialen Reizen) auftreten, eher als reflexive Reaktionen zu verstehen. Dementsprechend ist es wahrscheinlich, dass die Inhibition reflexiver Sakkaden in der Antisakkaden-Aufgabe und die Stärke des mimischen Schmerzausdrucks in einem solchen Kontext durch den gleichen reflexiven Mechanismus reguliert bzw. durch das gleiche inhibitorische „Gate“ gefiltert werden. Die Leistung des Stroop-Tests scheint hingegen von der Regulation durch ein anderes inhibitorisches „Gate“ abhängig zu sein, da hier eher höhere kognitive Prozesse eine Rolle spielen.

Diese Interpretation wird ebenfalls von Befunden aus Bildgebungsstudien gestützt. So zeigt sich eine große Übereinstimmung der aktivierten Areale z.B. im Präfrontalkortex oder den Basalganglien, wenn man die Regulation von Schmerzmimik und die Ausführung der Antisakkaden-Aufgabe vergleicht (Ford, Goltz, Brown & Everling, 2005; Goldin et al., 2008; Kunz et al., 2011; Munoz & Everling, 2004). Beim Stroop hingegen kommt es hauptsächlich zur Aktivierung des anterioren Cingulums (ACC), der Insula und prämotorischen sowie inferior frontalen Arealen (Leung, Skudlarski, Gatenby, Peterson & Gore, 2000), die bei der Mimikregulation keine große Rolle zu spielen scheinen.

Der fehlende Zusammenhang zwischen dem UPPS und der Stärke des mimischen Schmerzausdrucks weist ferner darauf hin, dass die Inhibitionsmechanismen, die an Impulskontrolle beteiligt sind, ebenfalls nicht diejenigen sind, die die Schmerzmimik stark beeinflussen.

Als Fazit lässt sich festhalten, dass Inhibitionsmechanismen tatsächlich eine bedeutende Rolle bei der Regulation von Schmerzmimik zu spielen scheinen. Dies gilt aber nicht für alle Inhibitionsmechanismen per se, sondern bezieht sich spezifisch nur auf die Inhibition automatisierter, motorischer Reaktionen.

3.3 Studie II

Karmann, A. J., Maihöfner, C., Lautenbacher, S., Sperling, W., Kunz, M. (…). The role of prefrontal inhibition in regulating facial expressions of pain.

3.3.1 Theoretischer Hintergrund

Nachdem in Studie I der Inhibitionsmechanismus identifiziert wurde, der die Regulation von Schmerzmimik vornehmlich beeinflusst, sollte im Rahmen von Studie II geklärt werden, welches Gehirnareal diese Inhibition vermittelt. Wie bereits in 2.2.1 beschrieben, betont eine fMRT-Studie (Kunz et al., 2011) in diesem Kontext die Rolle des medialen Präfrontalkortex (mPFC). Diese fMRT-Daten lassen jedoch keine Aussage darüber zu, ob präfrontale Aktivität tatsächlich kausal an der Inhibition des mimischen Schmerzausdrucks beteiligt ist.

Inzwischen ist eine Überprüfung solcher Annahmen mithilfe der sogenannten repetitiven transkraniellen Magnetstimulation (rTMS) möglich. Durch die wiederholte Applikation magnetischer Impulse am Schädel kann bei niedrigfrequenter rTMS (≤ 1 Hz) die neuronale Aktivität begrenzter Gehirnareale reduziert oder sogar gestört werden (Chen et al., 1997; Gangitano et al., 2002; Maeda, Keenan, Tormos, Topka & Pascual-Leone, 2000; Wassermann, 1998). Diese Tatsache sollte sich nun in Studie II zunutze gemacht werden, um die Erregbarkeit des mPFC (als Ausgangspunkt der Suche relevanter Areale) zu reduzieren und somit die Rolle präfrontaler Aktivität bei der Inhibition des mimischen Schmerzausdrucks zu überprüfen. Dementsprechend erfolgte die Erfassung von Schmerzmimik sowohl nach niedrigfrequenter rTMS (1Hz) als auch nach einer Sham-Stimulation. Sollte sich mediale präfrontale Aktivität tatsächlich inhibitorisch auf den mimischen Schmerzausdruck wirken, sollte sich während einer Phase reduzierter präfrontaler Erregbarkeit (ausgelöst durch 1 Hz-rTMS) eine erhöhte Schmerzmimik im Vergleich zur Sham-Bedingung verzeichnen lassen.

Um sicherzustellen, dass die beobachteten Effekte nicht auf eine durch rTMS veränderte Schmerzempfindung zurückzuführen sind, erfolgte in Studie II zudem der Vergleich von subjektiv berichteter Schmerzintensität zwischen rTMS und Sham-Stimulation. Ausgehend davon, dass für rTMS über dem mPFC – im Gegensatz zu rTMS über dem dorsolateralen präfrontalen und motorischen Kortex – keine Wirkung auf die

Schmerzempfindung bekannt ist (vgl. Mylius, Borckardt & Lefaucheur, 2012), wurden allerdings keine Unterschiede zwischen der rTMS und Sham-Stimulation erwartet.

3.3.2 Methode

In Studie II setzte sich die Stichprobe aus 19 weiblichen und 16 männlichen gesunden Erwachsenen zusammen (Alter: M = 25,7; SD = 9,8 Jahre). Das Experiment bestand aus drei Sitzungen. Die erste fand in den Labors der Universität Bamberg statt und diente als Trainingssitzung, in der die Teilnehmer mit dem Ablauf des in den nächsten Sitzungen folgenden Experiments bekannt gemacht wurden. Die folgenden zwei Termine fanden im Universitätsklinikum Erlangen statt und unterschieden sich nur darin, welche Stimulation zu Beginn der Sitzung über dem mPFC appliziert wurde. In einer Sitzung erhielten die Probanden für 20 Minuten eine niedrigfrequente rTMS (1 Hz; 90% der individuellen Motorschwelle; 1200 Impulse; Stimulationsort: FPz). In der anderen Sitzung erfolgte nur die Simulation einer Stimulation (Sham-Stimulation), indem mit einer Spule gleicher Größe und gleichen Aussehens zwar die gleichen Geräusche, aber keine tatsächlichen magnetischen Impulse abgegeben wurden. Die Stimulation erfolgte in beiden Fällen mithilfe eines Dantec MagPro MC 125 Stimulators und flüssigkeitsgekühlten Achterspulen. Die Reihenfolge der Stimulation (rTMS, Sham) wurde über die Probanden und Geschlechter hinweg randomisiert.

In beiden Sitzungen erfolgte direkt nach der jeweiligen Stimulation die Messung des mimischen Schmerzausdrucks. Dabei wurden zunächst schmerzhafte Druckreize appliziert, gefolgt von einer schmerzhaften Heißwasserstimulation (vgl. 3.1.1). Nach jedem der Reize sollten die Probanden ihre subjektiv empfundene Schmerzintensität mithilfe einer numerischen Ratingskala (NRS; 0-100) angeben. Dabei entsprach „0“ „keinem Schmerz“ und „100“ „extrem starkem Schmerz“. Neben der Erfassung des subjektiven Selbstberichts erfolgte die FACS-Kodierung der Mimik bei allen Reizen. Zusätzlich zum *composite score* schmerzrelevanter Mimik wurde auf die gleich Art und Weise ein *composite score* schmerzirrelevanter Mimik gebildet. Dies diente dem Zweck festzustellen, ob die durch rTMS hervorgerufenen Veränderungen einen allgemeinen, unspezifischen Anstieg in der Aktivität der Gesichtsmuskulatur bedingen oder sich nur spezifisch auf die Schmerzmimik auswirken.

3.3.3 Ergebnisse

Varianzanalysen ergaben, dass nach niedrigfrequenter rTMS über dem mPFC – verglichen mit Sham-Stimulation – ein verstärkter mimischer Schmerzausdruck (und somit wahrscheinlich eine reduzierte Inhibition dessen) auftrat. Dieser Effekt konnte für beide Arten der Schmerzreize (Druck, Heißwasser) sowie beide *composite scores*

(schmerzrelevant, schmerzirrelevant) nachgewiesen werden. Eine Interaktion zwischen Stimulationsart und *composite score* zeigte, dass die schmerzrelevante Mimik in einen stärkeren Ausmaß anstieg als die schmerzirrelevante Mimik und sich die Differenz zwischen beiden Arten der Mimik nach rTMS verstärkte. Insgesamt war die schmerzrelevante Mimik zudem stärker ausgeprägt als die schmerzirrelevante Mimik. Im Gegensatz zur Schmerzmimik zeigte sich in der (Varianz-) Analyse des subjektiven Schmerzberichts kein Unterschied zwischen rTMS und Sham-Stimulation.

3.3.4 Diskussion

In Studie II konnte klar gezeigt werden, dass eine Reduktion präfrontaler Erregbarkeit – induziert durch niedrigfrequente rTMS (1 Hz) über dem mPFC – mit einer verstärkten Schmerzmimik einhergeht. Dieses Ergebnis bestätigt die Vermutung aus vorherigen Bildgebungsstudien (Goldin et al., 2008; Kunz et al., 2011), dass es aufgrund von präfrontaler Aktivierung zu einer Inhibition des mimischen Schmerzausdrucks kommt. Gemeinsam mit den Erkenntnissen aus Studie I erhärten diese Befunde die Annahme, dass die Stärke des mimischen Schmerzausdrucks durch inhibitorische Kontrolle (mit-) bestimmt wird und rücken dabei präfrontale Areale als Kontrollinstanz in den Vordergrund.

Bei genauerer Betrachtung der Daten ließ sich zudem feststellen, dass diese präfrontale Inhibition allgemein – also unabhängig von der Art des zugrundeliegenden Schmerzreizes – zu erfolgen scheint. So bewirkte niedrigfrequente rTMS eine verstärkte Schmerzmimik bei sowohl schmerzhafter Hitze- als auch Druckstimulation.

Die rTMS schien sich auch ähnlich auf beide Arten der Mimik (schmerzrelevant/ schmerzirrelevant) auszuwirken. So ergab sich nach rTMS sowohl eine erhöhte schmerzrelevante Mimik, als auch ein Anstieg in schmerzirrelevanter Mimik. Allerdings bewirkte die rTMS eine stärkeren Anstieg der schmerzrelevanten Mimik als er bei schmerzirrelevanter Mimik zu verzeichnen war und die Differenz zwischen beiden Arten der Mimik verstärkte sich nach rTMS. Demnach scheint eine präfrontale Aktivierung sowohl das „Signal“ (schmerzrelevante Mimik) als auch das „Rauschen“ (schmerzirrelevante Mimik) des mimischen Schmerzausdrucks zu reduzieren. Der primäre Fokus des Mechanismus scheint allerdings auf der Regulation des „Signals“ und somit der Stärke bedeutender mimischer Ausdrücke zu liegen, anstatt nur auf einer unspezifischen, allgemeinen Reduktion muskulärer Aktivität.

Eine weitere Charakterisierung des vorliegenden präfrontalen Inhibitionsmechanismus ermöglichte der Befund, dass sich nach rTMS eine erhöhte Schmerzmimik ergab, ohne dass der subjektive Schmerzbericht signifikant verändert wurde. Die beobachtbaren Unterschiede in der Schmerzmimik scheinen demnach durch die (rTMS-) Modulation

eines Systems hervorgerufen worden zu sein, das spezifisch die Schmerzmimik und nicht die Schmerzempfindung an sich reguliert.

Zusammenfassend lässt sich demnach festhalten, dass eine Reduktion der präfrontalen kortikalen Erregbarkeit (mittels rTMS über mPFC) eine erhöhte Schmerzmimik bedingte, ohne dabei den Schmerzbericht zu verändern. Dieses Ergebnis untermauert stark die These, dass präfrontale inhibitorische Mechanismen den mimischen Schmerzausdruck herabregulieren und weist darauf hin, dass dies unabhängig von Veränderungen der zugrundeliegenden Schmerzempfindung geschieht.

3.4 Studie III

Karmann, A. J., Lautenbacher, S., Bauer, F., Kunz, M. (2014). The influence of communicative relations on facial responses to pain: does it matter who is watching? *Pain Research & Management* 19 (1), S. 15–22.

3.4.1 Theoretischer Hintergrund

Wie bereits in Punkt 2.2.4 beschrieben, existieren Hinweise darauf, dass die Inhibition des mimischen Schmerzausdrucks – ähnlich wie bei anderen Affektzustände auch – sozialen Einflüssen unterliegt. Bisher mangelt es allerdings an systematischen, FACS-basierten Untersuchungen, die bestimmen hätten können, welche Veränderungen die Anwesenheit unterschiedlich vertrauter Interaktionspartner in der Schmerzmimik von Erwachsenen hervorruft. Dies sollte nun in Studie III behoben werden.

Bei der Untersuchung solcher Effekte muss berücksichtigt werden, dass diese sowohl von Merkmalen des Senders als auch des Empfängers mimischer Botschaften beeinflusst werden könnten. So scheint das Ausmaß der Inhibition, das je nach Interaktionspartner auf die Schmerzmimik ausgeübt wird, zum einen vom Geschlecht des Senders abzuhängen. Hinweise darauf liefern Untersuchungen zum mimischen Ausdruck von anderen Affektzuständen. Gegenüber Fremden scheinen demnach Frauen – im Vergleich zu Männern – Freude und Lachen offener zu zeigen, wobei sie den Ausdruck negativer Gefühle wie Wut und Aggression eher inhibieren (Cole, 1986; Davis, 1995; Hall, 1990; Kring, 2000; LaFrance, Hecht & Paluck, 2003; Saarni, 1984). Studien zum verbalen Schmerzbericht deuten an, dass neben dem Geschlecht des Senders auch dem Geschlecht des Empfängers eine solche modulierende Rolle zukommen könnte. So beschrieben Männer ihren Schmerz als weniger stark, wenn eine weibliche Versuchsleiterin anwesend war (Aslaksen, Myrbakk, Høifødt & Flaten, 2007; Kallai, Barke & Voss, 2004; Levine & Simone, 1991). Dementsprechend ist es möglich, dass das Geschlecht des Empfängers nicht nur eine Modulation des verbalen Schmerzberichts hervorruft, sondern auch die Inhibition des mimischen Schmerzausdrucks beeinflusst.

Insgesamt weist die momentane Befundlage also darauf hin, dass das Geschlecht sowohl des Senders als auch des Empfängers das Ausmaß an Inhibition über die Schmerzmimik beeinflussen könnte und somit berücksichtigt werden sollte.

Bei der Betrachtung aller bisherigen Ergebnisse fällt zudem auf, dass bis dato nur untersucht wurde, inwiefern die Anwesenheit eines Beobachters die Stärke des mimischen Ausdrucks moduliert. Es wäre aber auch möglich, dass sich die Zusammensetzung der Muskelbewegungen über unterschiedliche Situationen hinweg verändert. Eine minimale Veränderung in der Zusammensetzung könnte dabei bereits dafür sorgen, dass sich die Botschaft des Ausdrucks verändert (indem z.B. das Verhältnis sensorisch-diskriminativer und affektiver Komponenten abweicht). Deshalb ist es sinnvoll, bei einer entsprechenden Untersuchung auch mögliche Veränderungen in der Zusammensetzung der Muskelbewegungen zu überprüfen.

Somit war das Ziel von Studie III bei gesunden Erwachsenen die Stärke (Inhibition) sowie die Zusammensetzung des mimischen Schmerzausdrucks in drei verschiedenen Bedingungen zu untersuchen: alleine, in Anwesenheit eines Versuchsleiters (Fremder) und in Anwesenheit des Partners (Vertrauter). Zusätzlich wurden dabei das Geschlecht der Versuchsperson sowie des Versuchsleiters berücksichtigt.

3.4.2 Methode

In Studie III bestand die Stichprobe aus 126 gesunden Probanden (63 heterosexuelle Paare; Alter: M = 39,9; SD = 13,5 Jahre). Im Verlauf des Experiments durchliefen die Teilnehmer drei Bedingungen, in denen die zuvor beschriebene Stimulation mit phasischen Hitzereizen (Kontaktthermode) erfolgte. In einer der Bedingungen waren sie während der Stimulation alleine im Zimmer, in einer anderen gegenüber vom Versuchsleiter und einer weiteren gegenüber von ihrem Partner platziert. Ähnlich wie in Studie I sollten die Probanden in allen drei Bedingungen nach jedem der Reize mithilfe einer VAS (100 mm; Kodierung siehe 3.2.2) ihre subjektiv empfundene Scherzintensität ausdrücken. Zusätzlich zum Selbstbericht erfolgt die FACS-Kodierung der Mimik bei allen Reizen.

Um festzustellen, ob sich die Inhibition von Schmerzmimik über die Bedingungen hinweg veränderte, wurden die folgenden Analysen durchgeführt. Zum einen wurde erfasst, ob sich die Art des mimischen Ausdrucks veränderte, indem die Verteilung der einzelnen AUs mittels Chi^2-Test zwischen den Bedingungen verglichen wurde. Zum anderen erfolgte eine Analyse der Veränderungen in berichteter Schmerzintensität und der Stärke des mimischen Ausdrucks (*composite* score) über die Bedingungen hinweg. Abschließend wurde untersucht, ob die Veränderungen in der Stärke des mimischen Ausdrucks

(Differenzen: Partner – Alleine; Versuchsleiter – Alleine) vom Geschlecht – sowohl der Versuchsperson als auch des Versuchsleiters – abhingen.

3.4.3 Ergebnisse

Ein Vergleich der Verteilung der AUs zeigte keine Unterschiede zwischen den Bedingungen auf. Demnach scheint die Zusammensetzung des mimischen Ausdrucks bei Schmerz über unterschiedliche soziale Kontexte hinweg konstant zu bleiben. Die Varianzanalyse zur Untersuchung der Unterschiede in der Stärke des mimischen Ausdrucks ergab jedoch signifikante Unterschiede zwischen den Bedingungen. So zeigten die Probanden im Vergleich zu den anderen Bedingungen in Anwesenheit des Partners eine erhöhte Schmerzmimik, was auf eine reduzierte Inhibition der Schmerzmimik in diesem Kontext hinweist. Die subjektiv berichtete Schmerzintensität unterschied sich hingegen nicht zwischen den Bedingungen. Die erhöhte Schmerzmimik in Anwesenheit des Partners ergab sich dabei unabhängig vom Geschlecht. In Anwesenheit des Versuchsleiters hingegen zeigten sich unterschiedliche Ergebnisse je nach Geschlecht der Versuchsperson. So inhibierten nur Frauen ihre Schmerzmimik in Anwesenheit des Versuchsleiters (signifikant reduzierte Schmerzmimik). Die Veränderung der Schmerzmimik war jedoch unabhängig vom Geschlecht des Versuchsleiters.

3.4.4 Diskussion

In Studie III sollte erfasst werden, wie die Anwesenheit unterschiedlich vertrauter Personen (allein, Partner, Versuchsleiter) die Zusammensetzung und Inhibition von Schmerzmimik bei gesunden Erwachsenen beeinflusst. Es zeigte sich, dass Schmerz – unabhängig von der Vertrautheit zwischen Sender und Empfänger – durch die gleichen Elemente der Mimik kommuniziert wurde. Die Mimik setzte sich dabei aus den üblichen Muskelbewegungen zusammen: dem Herunterziehen der Brauen (AU4), der Anspannung der Muskeln um die Augen (AU6/7) und der Kontraktion des Levator Muskels (AU9/10). In Anbetracht der Tatsache, dass die Schmerzmimik als solche erkennbar sein muss, um ihre Funktion in „interaction“ und „transaction“ zu erfüllen (Hadjistavropoulos et al., 2011; Williams, 2002), scheint die Konstanz dieser Zusammensetzung durchaus plausibel. Eine fundamentale Veränderung der Zusammensetzung der Schmerzmimik je nach Kontext könnte diese Erkennbarkeit potentiell gefährden und sich somit nachteilig auf die Kommunikation auswirken.

Bezüglich der Hauptfragestellung zeigte sich, dass die Stärke (Inhibition) des mimischen Ausdrucks stark zwischen den Bedingungen variierte und demnach von der Vertrautheit zwischen Sender und Empfänger beeinflusst zu sein schien. So schien in Anwesenheit des Partners der mimische Schmerzausdruck weniger inhibiert zu werden, was sich in

einer erhöhten Schmerzmimik niederschlug. Die Anwesenheit des Versuchsleiters rief hingegen (bei Frauen) eine tendenziell reduzierte Schmerzmimik hervor, was darauf hinweist, dass in dieser Situation mimische Inhibition stärker ausgeprägt war. Zusammen mit Befunden aus Studien mit Kindern (Vervoort et al., 2008; Vervoort et al., 2011) weisen diese Ergebnisse demnach darauf hin, dass der mimische Ausdruck von Schmerz ähnlichen sozialen Regeln („social display rules“) folgt wie der Ausdruck anderer Affektzustände. So scheint es, ähnlich wie bei anderen Affektzuständen, gegenüber einem Vertrauten – dem Partner (vorliegende Studie) oder den Eltern (Vervoort et al., 2008; Vervoort et al., 2011) – eher angemessen zu sein seinem Schmerz über die Mimik Ausdruck zu verleihen als in Anwesenheit eines Unbekannten oder allein.

Die Tatsache, dass nur Frauen gegenüber dem Versuchsleiter ihre Schmerzmimik reduzierten, weist ferner darauf hin, dass diese Regeln für Männer und Frauen unterschiedlich ausgeprägt zu sein scheinen. Dies steht im Einklang mit früheren Berichten, dass Frauen im Beisein Fremder positive Affektzustände in einem stärkeren Ausmaß mimisch kommunizieren und negative wie z.B. Ärger dagegen eher verbergen (Cole, 1986; Davis, 1995; LaFrance et al., 2003; Saarni, 1984; Underwood et al., 1992). Im Widerspruch zu vorherigen Studien steht hingegen, dass das Geschlecht des Versuchsleiters keine ausschlaggebenden Effekte auf die Veränderung in der Schmerzmimik hatte. Diese Divergenz lässt sich möglicherweise darauf zurückführen, dass die bisherigen Befunde nur aus der Untersuchung des verbalen Schmerzberichts stammen (Aslaksen et al., 2007; Kallai et al., 2004; Levine & Simone, 1991). Da die Mimik bekanntermaßen weniger leicht zu beeinflussen ist als der verbale Schmerzbericht (Craig et al., 2011), könnten sich solche Geschlechtseinflüsse im verbalen Schmerzbericht niederschlagen, während die Mimik unverändert bleibt.

Zusammenfassend lässt sich festhalten, dass Schmerz – unabhängig von der Vertrautheit zwischen Sender und Empfänger – über die gleichen Elemente der Mimik kommuniziert wird, was die Erkennbarkeit der charakteristischen Schmerzmimik zu erhalten scheint. Das Ausmaß mimischer Inhibition scheint hingegen gemäß sozialer Regeln auf den Interaktionspartner angepasst zu werden. So wird die Inhibition von Schmerzmimik gegenüber vertrauten Personen scheinbar gelockert, was damit zusammenhängen könnte, dass diese potentiell eher hilfsbereit sind. Eine verstärkte Inhibition von Schmerzmimik scheint sich hingegen in Anwesenheit eines Unbekannten zu ergeben. Dies ist allerdings nur bei Frauen der Fall, was durch unterschiedliche Lernprozesse bei Männern und Frauen bedingt sein könnte.

4. Übergreifende Diskussion

Ziel der vorliegenden Arbeit war es, die Beteiligung von Inhibitionsmechanismen an der Regulation von Schmerzmimik zu bestätigen und den beteiligten spezifischen Inhibitionsmechanismus genauer zu charakterisieren. Die Umsetzung dessen umfasste die Untersuchung unterschiedlicher Aspekte der Inhibition von Schmerzmimik, um sowohl psychosoziale als auch neurobiologische Einflussfaktoren beurteilen zu können und somit ein besseres Verständnis dieses Regulationsmechanismus und dessen Bedeutsamkeit zu erreichen.

Zu diesem Zweck wurde in Studie I zunächst ermittelt, welche Art von Inhibitionsmechanismus für die Regulation von Schmerzmimik zuständig ist. Dabei konnte nachgewiesen werden, dass die Stärke des mimischen Schmerzausdrucks durch die Leistung in der Antisakkaden-Aufgabe (Indikator motorischer Inhibition) vorhergesagt werden kann. Dies war nicht der Fall, wenn die Leistung im Stroop-Test (Indikator von kognitiver und Verhaltensinhibition) oder der UPPS (selbst-berichtete Impulskontrolle) als Prädiktor verwendet wurden. Demnach scheint vor allem die Inhibition von automatisierten, motorischen Reaktionen bei der Regulation von Schmerzmimik eine Rolle zu spielen. Studie II befasste sich anschließend mit den neurobiologischen Grundlagen der Inhibition von Schmerzmimik. Hier konnte gezeigt werden, dass eine durch rTMS bedingte präfrontale Aktivitätsreduktion mit einer erhöhten Schmerzmimik einherging. Dies deutet darauf hin, dass präfrontale Aktivität maßgeblich an der Inhibition von Schmerzmimik beteiligt ist. In Studie III wurde zuletzt ermittelt, ob die Inhibition des mimischen Schmerzausdrucks bei Erwachsenen von psychosozialen Einflüssen – hier der Vertrautheit der Interaktionspartner – abhängt. Tatsächlich deuten die Daten an, dass die Inhibition von Schmerzmimik in Anwesenheit des Partners reduziert und im Beisein eines Versuchsleiters (zumindest bei Frauen) verstärkt wird.

Diese, in den Studien I-III gewonnenen Erkenntnisse, lassen nun eine Beurteilung sowie eine genauere Beschreibung des bei der Regulation von Schmerzmimik beteiligten Inhibitionsmechanismus und dessen Einflussgrößen zu. Diese Charakteristika sollen im Folgenden in einem Modell zusammengefasst werden, wobei die Erkenntnisse der einzelnen Studien schrittweise hinzugenommen werden, um das Modell zu ergänzen. Im Anschluss erfolgt eine kritische Diskussion des untersuchten Mechanismus sowie der Rahmenbedingungen bei der Erhebung der vorliegenden Daten.

4.1 Modell der Inhibition von Schmerzmimik

Als Grundlage des Modells fungieren zunächst die bisherigen Erkenntnisse bezüglich mimischer Schmerzkommunikation. Wie in Abbildung 1 verdeutlicht, steht demnach am

Beginn einer mimischen Schmerzreaktion die nozizeptive Reizung durch einen Schmerzreiz. Dieser wird vom Organismus verarbeitet und es kommt zu einer automatischen, reflexartigen Generierung der Mimikreaktion (Craig et al., 2010; Hadjistavropoulos et al., 2011)(vgl. Abbildung 1). In diesem Schritt muss weder eine bewusste Verarbeitung erfolgen, noch sind aufwändige, ressourcenfordernde Verarbeitungsschritte von Nöten. Da bereits Säuglinge spezifische mimische Schmerzreaktionen zeigen können (Grunau & Craig, 1987; Williams, 2002), ist ferner davon auszugehen, dass es sich bei diesem Vorgang um eine biologisch vorbereitete Reaktion handelt, die primär durch die Eigenschaften des Stimulus bestimmt wird. Aus den Befunden von Kunz et al. (2011) lässt sich entnehmen, dass diese interne Neigung mit einer Mimikreaktion auf Schmerzen zu reagieren möglicherweise von einem Netzwerk hervorgerufen wird, das sich aus primär motorischen und schmerzverarbeitenden Arealen (primär somatosensorischer Kortex, Insula und ACC) zusammensetzt.

Wie andere reflexive Antworten auch (z.B. stress-induzierte Reduktion des Wegziehreflexes (Ford & Finn, 2008); Startle-Potenzierung durch negative Emotionen (Bradley, Silakowski & Lang, 2007)), kann diese automatische Reaktion allerdings modifiziert werden. Die Daten der bereits vorgestellten fMRT-Studie (Kunz et al., 2011) wiesen darauf hin, dass eine solche Modifikation durch Inhibitionsmechanismen bedingt sein könnte. So zeigte sich, dass die Aktivität eines fronto-striatalen Netzwerks, dessen Areale bekanntermaßen an motorischer Inhibition beteiligt sind (Aron et al., 2007; Ridderinkhof et al., 2004), mit einer Reduktion von Schmerzmimik assoziiert war. Demnach scheint es zu einer Inhibition der automatisch generierten Mimikreaktion zu kommen, was die Stärke des mimischen Schmerzausdrucks beeinflusst (vgl. Abbildung 1). Die Ergebnisse aller im Rahmen dieser Arbeit erfolgten Studien (I-III) untermauern nun diese Hypothese und lassen eine genauere Charakterisierung des beteiligten Inhibitions-mechanismus und von dessen Einflussgrößen zu.

4.1.1 Motorische Inhibition als spezifischer Regulationsmechanismus

So konnte Studie I zunächst darüber Aufschluss geben, welcher Inhibitionsmechanismus für die Regulation von Schmerzmimik von besonderer Bedeutung ist. Es zeigte sich, dass die Stärke des mimischen Schmerzausdrucks von der Leistung in der Antisakkaden-Aufgabe vorhergesagt werden konnte. Eine gute Leistung in dieser Aufgabe zeichnet sich durch eine ausgeprägte Fähigkeit aus, automatische, okulomotorische Orientierungs-reaktionen (Sakkaden) in Richtung eines plötzlich auftauchenden, peripheren Stimulus inhibieren zu können. Je besser diese Fähigkeit in Studie I ausgeprägt war, desto weniger drückten die Probanden ihren Schmerz über die Mimik aus. Dieser signifikante Zusammenhang zwischen der Stärke des mimischen Schmerzausdrucks und der

Inhibitionsleistung in der Antisakkaden-Aufgabe weist darauf hin, dass beide Prozesse über den gleichen Mechanismus bzw. über das gleiche inhibitorische „Gate“ reguliert werden, welches vornehmlich für die Inhibition automatischer, motorischer Reaktionen zuständig ist.

Dass die Inhibition der Schmerzmimik hauptsächlich und spezifisch durch diesen Inhibitionsmechanismus bestimmt wird, zeigte die Tatsache, dass die Leistung im Stroop-Test sowie das Persönlichkeitsmerkmal „Impulskontrolle“ (erfasst durch die UPPS) die Stärke des mimischen Schmerzausdrucks nicht vorhersagen konnten. Demnach scheint der an der Regulation von Schmermimik beteiligte Inhibitionsmechanismus wenig von inhibitorischen „Gates“ abhängig zu sein, die bei eher höheren, kognitiven Prozessen (wie im Stroop-Test) oder bei der Impulskontrolle (UPPS) eine Rolle spielen.

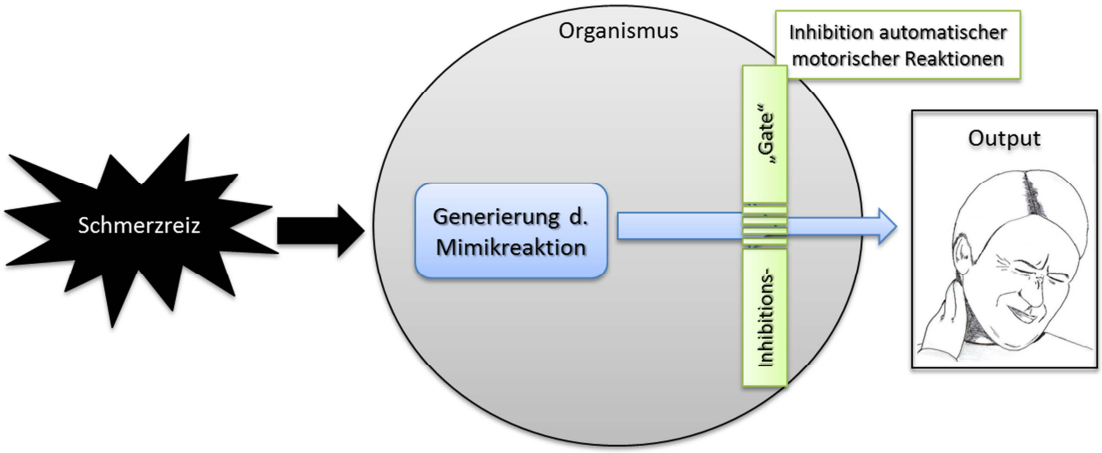

Abbildung 1: Modell der Inhibition von Schmerzmimik nach Studie I

Die nach den Vorbefunden von Kunz et al. (2011) getroffene Aussage kann somit durch die Ergebnisse von Studie I spezifiziert werden, was in dem in Abbildung 1 illustrierten Modell mündet. Demnach scheint die automatisch generierte Mimikreaktion insofern modifiziert werden zu können, dass motorische Inhibitionsmechanismen regulieren, wie viel dieser Reaktion tatsächlich nach außen getragen wird. Es erfolgt also eine Inhibition des automatisch generierten motorischen Plans, dessen Ausprägung im Endeffekt bestimmt, wie stark der mimische Schmerzausdruck präsentiert wird.

4.1.2 Aktivierung des Inhibitionsmechanismus durch präfrontale Areale

Nachdem in Studie I festgestellt wurde, welcher Inhibitionsmechanismus die Regulation von Schmerzmimik vornehmlich beeinflusst, sollte im Rahmen von Studie II geklärt werden, welche Gehirnareale diese Inhibition vermitteln. In der fMRT-Studie von Kunz et al. (2011) war eine reduzierte Schmerzmimik hauptsächlich mit der Aktivierung eines frontostriatalen Netzwerks – bestehend aus medialem Präfrontalkortex (mPFC) und

Nucleus Caudatus – assoziiert, was diese Areale als vermittelnde Kandidaten in den Vordergrund rückte. In Studie II konnte nun mittels non-invasiver Aktivitätsreduktion des mPFC (via rTMS) gezeigt werden, dass präfrontale Aktivierungsänderungen tatsächlich entscheidende Veränderungen in der Stärke des mimischen Schmerzausdrucks hervorrufen können. Die Tatsache, dass eine präfrontale Aktivitätsreduktion zu einer erhöhten Schmerzmimik führte, untermauert ferner die Annahme, dass präfrontale Areale maßgeblich daran beteiligt sind, eine Inhibition von Schmerzmimik zu vermitteln. Die durch rTMS hervorgerufene präfrontale Aktivitätsreduktion schien demnach eine Reduktion inhibitorischer Kontrolle herbeizuführen, was eine „Freisetzung" der Schmerzmimik bedingte.

Nach Studie II kann das Modell der Inhibition von Schmerzmimik folglich um die Aktivität präfrontaler Areale ergänzt werden (siehe Abbildung 2). Demnach kommt es zu einer „Ausgangskontrolle" der automatisch generierten Mimikreaktion über ein „Inhibitionsgate", das für die Inhibition automatischer, motorischer Reaktionen zuständig ist. Dieses „Gate" und somit das Ausmaß der Inhibition über die Schmerzmimik wird dabei von der Aktivität präfrontaler Areale reguliert, was schlussendlich die Stärke des mimischen Schmerzausdrucks (mit-)bestimmt.

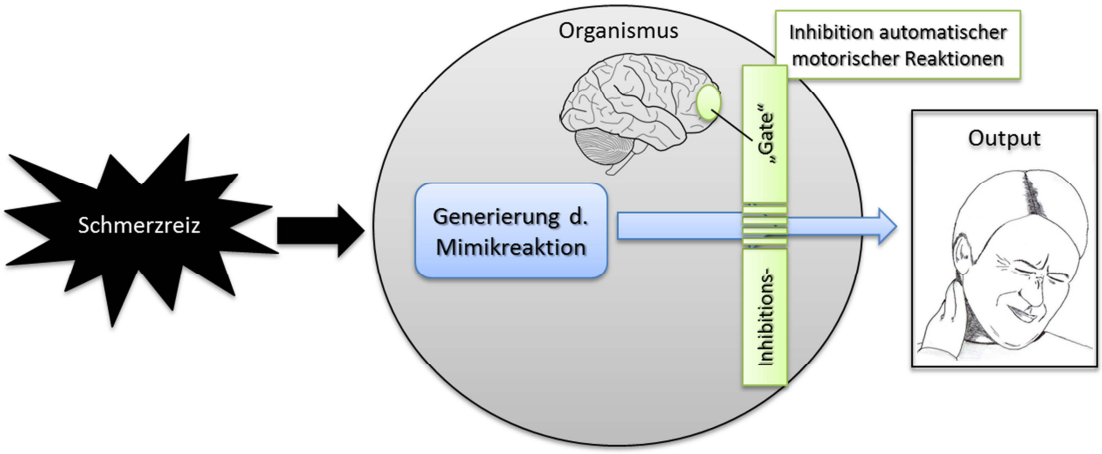

Abbildung 2: Modell der Inhibition von Schmerzmimik nach Studie I + II

Diese Interpretation steht auch im Einklang mit Befunden zur Entwicklung des mimischen Schmerzausdrucks. Wie bereits erwähnt, geht man von einer angeborenen Fähigkeit zur mimischen Darstellung unterschiedlicher Affektzustände (u.a. auch Schmerz) aus (Craig et al., 2011; Ekman, 1999). In den ersten Lebensmonaten sind Mimikreaktionen noch recht unkontrolliert und eher als reflexiv zu betrachten (Craig et al., 2011). Im Laufe der Sozialisation entwickelt sich dann eine selektive Kontrolle der Mimik und die Fähigkeit, die Stärke des mimischen Ausdrucks an Umgebungsbedingungen anzupassen (Craig et al., 2010; Izard, 1971). Dieser Prozess geht mit einer Reifung präfrontaler Areale einher, die

sich von der frühen Kindheit bis hin ins Jugendalter zieht (Giedd et al., 1999; Gogtay et al., 2004). Die Reifung präfrontaler Areale würde demnach die Entwicklung einer inhibitorischen Kontrolle über die Schmermimik fördern bzw. erleichtern, was eine adaptiertere Mimik bei älter werdenden Kindern zur Folge hätte.

Wie in Abbildung 2 angedeutet, scheint sich diese präfrontale Inhibition allerdings nicht auf die Schmerzerfahrung und somit die Generierung der Mimikreaktion auszuwirken. Dies zeigte sich in Studie II darin, dass die verwendete rTMS nur einen Output der Schmerzerfahrung, nämlich den mimischen Schmerzausdruck, nicht aber einen anderen, den verbalen Schmerzbericht, veränderte. Somit schien die selektive Modulation präfrontaler Aktivität nicht die latente Variable (Schmerzerfahrung), sondern einen spezifischen Output (Schmerzmimik) zu modulieren. Dies bestätigt die bereits zuvor beschriebene, vermutete Rolle des untersuchten präfrontalen Inhibitionsmechanismus. Dieser scheint demnach nicht die Schmerzerfahrung und somit die Entstehung bzw. Generierung des mimischen Schmerzausdrucks an sich zu inhibieren, sondern als „Ausgangskontrolle“ zu fungieren. Bei dieser „Ausgangskontrolle“ erfolgt eine Inhibition des generierten motorischen Plans, die bestimmt, wie viel der generierten Mimikreaktion tatsächlich nach außen getragen wird.

4.1.3 Soziale Vertrautheit als Einflussfaktor auf die Inhibition von Schmerzmimik

In der Form, in der das Modell in Abbildung 2 dargestellt ist, bezieht es sich lediglich auf die internen Prozesse, die bei der Inhibition von Schmerzmimik ablaufen. Dass eine solch isolierte Betrachtung nicht ausreichend ist, verdeutlichen Befunde zur sozialen Modulierbarkeit des mimischen Ausdrucks anderer Affektzustände (Underwood et al., 1992; Wagner & Smith, 1991; Yarczower & Daruns, 1982; Zeman & Garber, 1996). So scheinen soziale Regeln („social display rules“) vorzugeben, dass die Stärke des mimischen Ausdrucks an den Interaktionspartner angepasst werden soll. In Anwesenheit Fremder scheint es demnach erforderlich, den mimischen Affektausdruck zu inhibieren (Underwood et al., 1992; Yarczower & Daruns, 1982), wohingegen diese inhibitorische Kontrolle im Beisein vertrauter Personen gelockert werden kann (Underwood et al., 1992; Wagner & Smith, 1991; Zeman & Garber, 1996). Zusammen mit Befunden aus Studien mit Kindern (Vervoort et al., 2008; Vervoort et al., 2011) weisen die Ergebnisse von Studie III nun darauf hin, dass der mimische Schmerzausdruck ähnlichen sozialen Regeln unterliegt. So zeigte sich, dass die Probanden in Anwesenheit eines Vertrauten (Partner) ihren Schmerz vermehrt über die Mimik zeigten und speziell Frauen ihren mimischen Schmerzausdruck reduzierten, wenn ein Unbekannter (Versuchsleiter) anwesend war.

Gemäß dieser Ergebnisse von Studie III lässt sich das Modell der Inhibition von Schmerzmimik um eine weitere Komponente ergänzen (vgl. Abbildung 3). So scheint das

Ausmaß inhibitorischer Kontrolle über die Schmerzmimik immer davon beeinflusst zu sein, in welchem Kontext sich die Person mit Schmerzen befindet. Je nach Vertrautheit der Interaktionspartner geben demnach erlernte soziale Regeln vor, wie stark die Inhibition von Schmerzmimik ausfallen soll. Auf diese Weise wird gewährleistet, dass es in Anwesenheit Unbekannter zu einer verstärkten Inhibition und somit zu einer sozial angemessenen reduzierten Schmerzmimik kommt. In Anwesenheit vertrauter Personen hingegen fördert eine Lockerung der inhibitorischen Kontrolle, dass Schmerz offener kommuniziert wird.

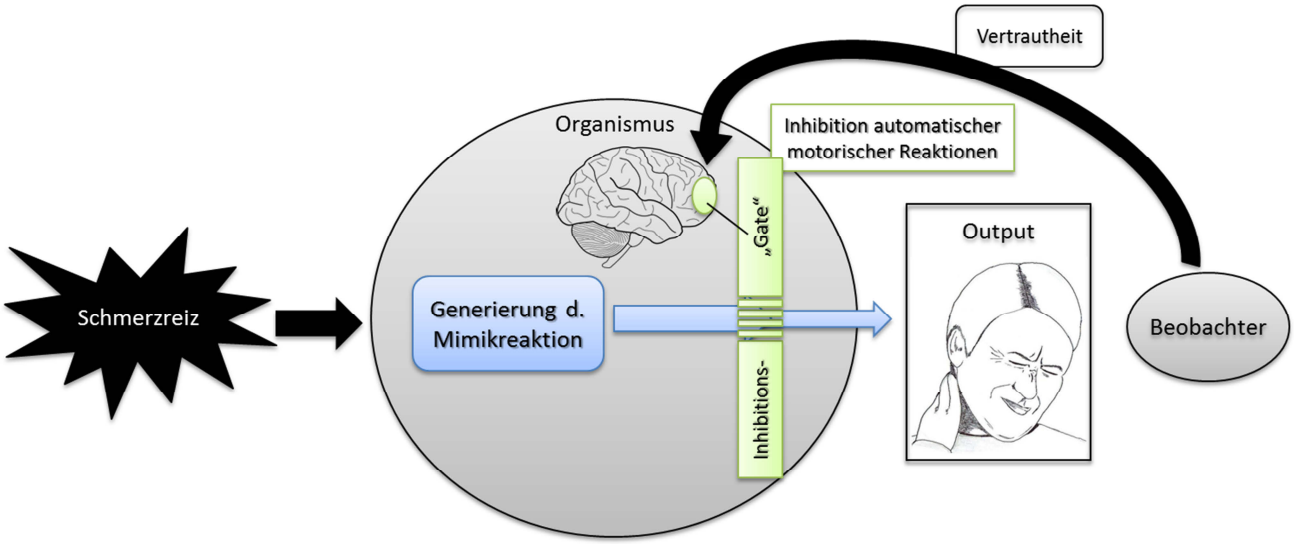

Abbildung 3: Modell der Inhibition von Schmerzmimik nach Studie I + II + III

Es sollte allerdings nicht davon ausgegangen werden, dass die Vertrautheit der Interaktionspartner und damit die genannten sozialen Regeln den einzigen psychosozialen Einfluss auf die Inhibition von Schmerzmimik darstellen. So konnte z.B. gezeigt werden, dass unterschiedliche Lernprozesse (wie Beobachtungslernen (Kunz, Faltermeier & Lautenbacher, 2012) und operantes Verstärkungslernen (Kunz, Rainville & Lautenbacher, 2011)) ebenfalls einen Einfluss darauf haben, wie stark Schmerzen über die Mimik kommuniziert werden. Demnach ist es wahrscheinlich, dass die individuelle Lerngeschichte sowie weitere Faktoren mitbestimmen, wie viel Inhibition zu einem bestimmten Zeitpunkt auf die Schmerzmimik ausgeübt wird. Diese Einflussfaktoren zu identifizieren und zu beurteilen war nicht das Ziel der vorliegenden Arbeit, und darum muss sich in zukünftiger Forschung bemüht werden. Der Vollständigkeit halber muss die Möglichkeit solcher Einflüsse allerdings bereits hier erwähnt werden.

4.2 Vor- und Nachteile der Inhibition von Schmerzmimik

Wie bei anderen Regulationsmechanismen auch, stellt sich die Frage nach dem Sinn und Zweck eines solchen Inhibitionsmechanismus. Warum ist die Entwicklung einer solchen

inhibitorischen Regulation vorteilhaft? Und existieren auf der anderen Seite auch Situationen, in denen sie von Nachteil sein kann?

Nach Sichtung des vorangegangenen Abschnitts wird schnell klar, worin die Vorteile einer inhibitorischen Regulation von Schmerzmimik liegen könnten. So lassen vorherige Befunde (Kleck et al., 1976; Saarni, 1984; Underwood et al., 1992; Vervoort et al., 2008; Vervoort et al., 2011) sowie die Ergebnisse von Studie III vermuten, dass bestimmte (formale) soziale Situationen ein gewisses Ausmaß an Inhibition des mimischen Ausdrucks erfordern, damit soziale Regeln nicht verletzt werden. Zudem scheint es auch an sich sinnvoll zu sein, den mimischen Schmerzausdruck und somit Anzeichen von Schwäche und Verletzlichkeit gegenüber Fremden zu inhibieren, da nicht vorhersehbar ist, ob es zu einer positiven oder negativen Reaktion kommen wird (Craig, 2004, 2009; Williams, 2002).

Die Inhibition von Schmerzmimik könnte neben dem Schutz der eigenen Person auch dem Schutz bestimmter Beobachter dienen. Es ist bekannt, dass das Betrachten von Schmerzmimik beim Beobachter eine ähnliche Gehirnaktivierung auslöst, wie sie auch bei eigenen Schmerzerfahrungen zu finden ist (Botvinick et al., 2005) und potentiell mit Stress verbunden ist (Crombez & Eccleston, 2002). Demnach könnte die Inhibition von Schmerzmimik auch aktiv eingesetzt werden, um den Beobachter (z.B. den Partner oder Familienangehörige) zu schonen bzw. nicht zu belasten (Crombez & Eccleston, 2002).

Ein weiterer Vorteil der Inhibition von Schmerzmimik hängt mit einer Hypothese zusammen, die erstmals von Darwin (1872) vorgebracht und unter dem Begriff der „Facial Feedback Hypothese“ weiter elaboriert wurde (Buck, 1980; Davis, Senghas & Ochsner, 2009; Larsen, Kasimatis & Frey, 1992; Strack, Martin & Stepper, 1988). Diese Hypothese besagt, dass ein ausgeprägter mimischer Ausdruck von Emotionen eine Verstärkung der emotionalen Erfahrung bedingt und eine Inhibition des mimischen Ausdrucks die emotionale Empfindung reduziert. Dementsprechend sollten schmerzhafte Erfahrungen durch eine Reduktion der Schmerzmimik als weniger intensiv empfunden werden. Erste Hinweise auf eine solche Modulierbarkeit der Schmerzempfindung stammen von Lanzetta, Cartwright-Smith und Kleck (1976). Sie konnten zeigen, dass es bei inhibierter Schmerzmimik – im Vergleich zu unveränderter und übertriebener Mimik – zu reduzierten subjektiven Schmerzintensitätsratings kam, was später auch repliziert werden konnte (Colby, Lanzetta & Kleck, 1977). Obwohl diese Befunde nicht ganz unstrittig sind (vgl. Prkachin, 2005), weisen sie darauf hin, dass einer der Vorteile der Inhibition von Schmerzmimik auch darin liegen könnte, die Schmerzempfindung abzuschwächen. Sollte sich dieser Zusammenhang als robust erweisen, könnte die Inhibition von Schmerzmimik aktiv im klinischen Setting angewendet werden, um die Intensität bestehender Schmerzen zu reduzieren.

Neben dieser Vielzahl an positiven Begleiterscheinungen scheint die Inhibition von Schmerzmimik allerdings auch negative Effekte nach sich ziehen zu können. So wurde berichtet, dass bei der Inhibition von mimischen Affektausdrücken eine erhöhte physiologische Erregung (gemessen mittels Hautleitfähigkeit) zu beobachten ist; was bei dauerhaftem Auftreten potentiell gesundheitsgefährdend wäre (Gross & Levenson, 1993, 1997). Zudem zeigte sich, dass die Inhibition des mimischen Ausdrucks von kognitiven Einbußen begleitet sein kann. In einer Studie dazu (Richards & Gross, 2000) konnten die Probanden die Details von emotionsauslösendem Material (Film, Bilder) sowie die eigene emotionale Erfahrung schlechter erinnern, wenn der mimische Ausdruck unterdrückt wurde. Bei der Interpretation dieser Ergebnisse bezüglich physiologischer Erregung und kognitiver Einbußen muss allerdings beachtet werden, dass sie in ihrem Anwendungsbereich limitiert sind. So erfolgte in all den genannten Studien eine Instruktion, die die Versuchspersonen dazu aufforderte, ihre Mimik aktiv und vollständig zu unterdrücken. Das heißt die beschriebenen Effekte dürften bei einer Inhibition, die nicht zu einer vollständigen Unterbindung, sondern nur zu einer Reduktion des mimischen Ausdrucks führt, gar nicht oder nur in reduziertem Maße auftreten. Da eine vollständige Unterdrückung des mimischen Schmerzausdrucks nur selten realisiert werden kann und somit im Alltag selten auftritt (Larochette, Chambers & Craig, 2006), sind diese Befunde eher als artifiziell und die Nachteile daher als weniger relevant einzustufen. Zudem ist eine instruierte und bewusste Inhibition potentiell mit einem höheren Aufwand an kognitiven Ressourcen verbunden, als das bei dem in der vorliegenden Arbeit untersuchten (nicht instruierten und nicht unbedingt bewussten) Inhibitionsmechanismus der Fall sein dürfte.

Zusätzlich zu den Effekten auf andere Systeme, könnte ein reduzierter mimischer Schmerzausdruck auch an sich nachteilig sein. Es ist bekannt, dass der mimische Schmerzausdruck im klinischen Setting oftmals auch in die Beurteilung der Schmerzintensität eines Patienten mit eingeht (Hadjistavropoulos et al., 2011; Williams, 2002). Kommt es also (durch die Anwesenheit Fremder, z.B. Klinikpersonal) zu einer Inhibition der Schmerzmimik, könnten Schmerzen unterschätzt und somit nicht ausreichend behandelt werden. Dies ist besonders dann problematisch, wenn die Personen mit Schmerzen noch nicht (Säuglinge) oder nicht mehr (z.B. Demenzpatienten) verbal über ihren Schmerz berichten können. Glücklicherweise scheint die Inhibition von Schmerzmimik gerade bei diesen Personen weniger stark ausgeprägt zu sein (Grunau & Craig, 1987; Johnston et al., 1993; Kunz et al., 2007), was potentiell nachteilige Effekte reduziert. In jedem Fall wäre es aber sinnvoll die Ergebnisse der vorliegenden Arbeit durch Schulungen an Klinikpersonal weiterzugeben und somit darüber aufzuklären, dass die Inhibition von Schmerzmimik vom jeweiligen Interaktionspartner beeinflusst wird. Dies

könnte die Interpretation vorliegender Informationen (z.B. bei einer Abweichung von Schmerzmimik und -bericht) verbessern und eine Unterversorgung bei Schmerzsymptomen verhindern.

4.3 Limitationen & Ausblick

Trotz der Tatsache, dass mithilfe der vorliegenden Arbeit die Inhibition des mimischen Schmerzausdrucks wesentlich besser charakterisiert werden kann, müssen die Implikationen teilweise limitiert werden. So muss zunächst angemerkt werden, dass alle Ergebnisse nur aus streng kontrollierten Settings stammen, in denen bei jungen, gesunden Probanden die Reaktion auf experimentelle Schmerzreize erfasst wurde. Demnach bleibt zu erforschen, inwiefern sich die Ergebnisse auf den mimischen Ausdruck von chronischem Schmerz und auf Alltagssituationen anwenden lassen.

Zudem erfolgte die Charakterisierung des Inhibitionsmechanismus in Studie I und II unter Ausgliederung des Einflusses unterschiedlicher Interaktionspartner. Dies war notwendig, um grundlegende Aussagen über den vorliegenden Inhibitionsmechanismus treffen zu können – muss allerdings in zukünftiger Forschung beachtet werden. So sollte zunächst Studie I mit unterschiedlichen Interaktionspartnern durchgeführt werden, um das Gewicht eines motorischen Inhibitionsmechanismus in unterschiedlichen sozialen Situationen einordnen zu können. Um sicherzustellen, dass das unterschiedliche Ausmaß an mimischer Aktivität in unterschiedlichen sozialen Settings auch wirklich auf Inhibitionsmechanismen zurückgeht, sollte außerdem Studie II um die Präsenz verschiedener Interaktionspartner erweitert werden. Sollten sich nach einer niedrig-frequenten rTMS (Reduktion mimischer Inhibition) keine Unterschiede mehr zwischen unterschiedlichen sozialen Situationen ergeben, könnte davon ausgegangen werden, dass der durch rTMS ausgesetzte Inhibitionsmechanismus dem Effekt der sozialen Situation zugrunde liegt.

Zuletzt bleibt anzumerken, dass diese Arbeit nur einen ersten Beitrag dazu leisten kann, die Regulation von Schmerzmimik besser zu verstehen. Der betonte Fokus der Arbeit lag darauf, die inhibitorischen Mechanismen dieser Regulation genauer zu untersuchen und es wurde nicht der Versuch unternommen ein ganzheitliches Modell zur Regulation von Schmerzmimik vorzulegen. In der Zukunft bedarf es daher auch der genaueren Untersuchung exzitatorischer Mechanismen, die in Situationen relevant sind, in denen eine verstärkte Schmerzmimik deutliche Vorteile bringt (z.B. in Foulsituationen im Profifußball) sowie deren Interaktion mit den hier behandelten Inhibitionsprozessen, um die Regulation der Schmerzmimik mit allen Facetten repräsentieren zu können.

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6. Anhang

Anhang 1: Studie I

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The role of inhibitory mechanisms in the regulation of facial expressiveness during pain

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ABSTRACT

Although it is assumed that inhibitory control plays a role in regulating the degree of facial expressiveness, so far the specific type of inhibitory mechanism involved has not been identified. The present study was designed to investigate the association between different types of inhibitory mechanisms and the degree of facial expressiveness.

Facial expressiveness during experimental pain was assessed using the Facial Action Coding System and facial electromyography (criterion variables). Different aspects of inhibitory functioning (Antisaccade task, Stroop task, questionnaire) were used as predictor variables.

The degree of facial expressiveness was significantly predicted by the performance in the Antisaccade, but not the Stroop task or the questionnaire. The higher the ability was to inhibit saccadic eye movements, the lower was the degree of facial expressiveness.

This data suggests that the degree of facial expressiveness is not regulated by inhibitory control in general, but specifically depends on inhibitory mechanisms regulating automatic motor responses.

1. Introduction

Facial expressions provide the possibility of conveying a large amount of information about inner affective states, thoughts and even motives of an individual to an observer (Craig, 2009; Craig, Prkachin, & Grunau, 2011; Ekman, 1999). Hence, they play an essential role in interpersonal relationships and social communication (Darwin, 1872; Halberstadt, Denham, & Dunsmore, 2001). In the context of distress (e.g. pain or fear), the function of facial expressions might even be fundamental. By signaling the experience to others, facial responses may elicit empathy and helping behavior, which may be crucial for survival (Botvinick et al., 2005; Williams, 2002).

Although facial expressions are known to be elicited rather automatically (Blair, 2003; Darwin, 1872), the degree to which inner affective states are actually displayed via the face varies substantially between individuals. Thus, even during strong emotional experiences, the degree of facial expressiveness ranges from stoicism, with almost no facial expressions shown, to high expressiveness (Gross & Levenson, 1993; Richards & Gross, 2000). Although these variations have been reported solidly, so far little is known about what kind of mechanisms are responsible for regulating the degree of facial expressiveness.

Interestingly, a recent fMRI study of our group on the neural regulation of facial expressiveness (Kunz, Chen, Lautenbacher, Vachon-Presseau, & Rainville, 2011) has created results that point toward one possible underlying mechanism. Here, it was shown that the degree of facial expressiveness during painful heat stimulation was associated with the activity of fronto-striatal circuits. The higher the activation was in medial prefrontal areas and in the caudate nucleus, the less strongly individuals displayed their pain via the face. Since these areas are known to be involved in motor inhibition (Aron et al., 2007; Ridderinkhof, van den Wildenberg, Segalowitz, & Carter, 2004), the most reasonable interpretation seems to be that motor inhibition plays a major role in the (down-)regulation of facial expressiveness; with an active inhibition resulting in a reduced degree of facial expressiveness.

The relevance of inhibition for the regulation of facial expressiveness can also be derived from developmental observations. Young children seem to have unfiltered access to the full repertoire of facial activities early in life (Ekman, 1999), but just gradually learn to selectively control and adjust their facial expressiveness according to situational demands (Craig, Versloot, Goubert, Vervoort, & Crombez, 2010; Izard, 1971). The fact that this acquired control is usually associated with a decrease in facial expressiveness (especially with regard to the display of negative affective

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states) (Izard, 1971) favors the idea of an active inhibition of facial responses. Thus, overtly displaying one's affective state seems to be the "default", which is learnt to be inhibited throughout socialization.

In the current study we have now tried to elaborate these ideas further by investigating whether the degree to which an individual expresses his/her pain is associated with measures of inhibitory functioning. In other words, if the regulation of facial expressiveness was indeed strongly influenced by inhibitory processes, the degree of facial expressiveness should be associated with other indicators of inhibition.

Before addressing the association of inhibitory functioning and facial expressiveness, it seems reasonable to first differentiate between different types of inhibitory mechanisms that might be relevant in this context. A common differentiation is made between "behavioral" and "cognitive" inhibition (Harnishfeger, 1995; Nigg, 2000). While "cognitive inhibition" refers to the action of controlling mental processes like memory or attention, "behavioral inhibition" corresponds to the ability of controlling or inhibiting pre-potent behavioral motor responses or impulses. This "behavioral inhibition" seems to be the most relevant category in our context, given that facial expressions are behavioral motor responses (Craig et al., 2011) and thus, seem likely to be governed by behavioral/motor inhibitory mechanisms. In order to determine variables that are hypothetically more or less closely related to facial expressiveness, "behavioral inhibition" was assessed using different approaches. Firstly, the Antisaccade task (Hallett, 1978) was chosen to determine the ability to inhibit a response which is very similar to facial expressions. Namely, the Antisaccade task measures occulomotor inhibition of an automatic orientation response/reflex (Nigg, 2000). The Stroop task (Stroop, 1935) was selected as a second, more distantly related measure. Although involving motor inhibition as well, the Stroop task additionally demands the higher cognitive process of decoding the word meaning (Nigg, 2000). Due to its cognitive components and to ease further understanding, the Stroop task will further be referred to as an indicator of "behavioral and cognitive inhibition". The choice of the Antisaccade and Stroop task was additionally founded in the fact that both represent well-established measures that indisputably belong to the battery commonly used to assess inhibitory functioning (Friedman & Miyake, 2004; Miyake et al., 2000). In order to assess "behavioral inhibition" on the level of dispositional personality variables and introduce this as a third, hypothetically most distantly related measure, the Impulsive Behavior Scale (UPPS; Whiteside & Lynam, 2001) was included in the current set of variables. The UPPS represents a well-elaborated tool for assessing impulsivity, which first established a subdivision of the trait into four distinct, but related factors. Its different dimensions have also been shown to be related to other indicators of inhibitory functioning (Gay, Rochat, Billieux, d'Acremont, & van der Linden, 2008; Roberts, Fillmore, & Milich, 2011). By precisely measuring all facets of impulsivity, this questionnaire, thus, seems to be best suited to identify a possible relationship between impulsivity and facial expressiveness.

In addition to inhibitory functioning, facial expressiveness was assessed using a standardized and experimentally controlled approach. As has successfully been done in our previous fMRI study (Kunz et al., 2011), experimental heat pain was used as method of affect-induction. This had the advantage of easily eliciting comparable levels of subjective experience across participants. In addition, two established methods to assess and quantify facial expressiveness were applied. On the one hand, we used the Facial Action Coding System (FACS; Ekman & Friesen, 1978), as has been done in most studies assessing the facial response to pain (for a review see Craig et al., 2011; Hadjistavropoulos et al., 2011). Moreover, electromyography (EMG) was conducted over the orbicularis oculi muscle (which is functionally the most prominent muscle in the response to pain; Prkachin, 1992) for a better resolution of the measurement than FACS can guarantee. Using these two complementary measures should enable a thorough assessment of the association between facial expressiveness and inhibitory functioning.

It has to be noted that participants were deliberately not instructed to inhibit facial expressiveness. The measurement, thus, differed from the measures of inhibitory functioning given that there was no clearly stated necessity to recruit inhibitory processes. However, as suggested by previous results (Karmann, Lautenbacher, Bauer, & Kunz, 2014; Kleck et al., 1976; Saarni, 1984; Underwood, Coie, & Herbsman, 1992; Vervoort et al., 2008, 2011), most social situations require the continuous inhibition of too frank expressions of (negative) internal states because otherwise social rules might be violated. Only in the presence of very intimate persons, this inhibitory control might be weakened (Karmann et al., 2014; Vervoort et al., 2008). Therefore, inhibition of facial expression was not subject to further instructions because inhibitory control was supposed to be sufficiently activated.

In summary, our aim was to investigate whether the degree of facial expressiveness (in response to painful stimulation) is related to inhibitory functioning (Antisaccade, Stroop task, UPPS). We hypothesized a substantial (negative) association between the degree of facial expressiveness and the performance in the Antisaccade task (hypothetically more closely related task). In contrast, the (negative) association with the performance in the Stroop task as well as with the UPPS was hypothesized to be more marginal; given that these two variables are hypothetically more distantly related to facial expressiveness.

2. Materials and methods

2.1. Participants

The 49 participants (24 females; M = 22.2 years; SD = 3.1) of the current study were recruited at the University of Bamberg by bulletins put up throughout campus. Individuals with chronic pain, psychological or physical illnesses or such taking psychotropic drugs or analgesics were excluded from participation. Furthermore, we only included participants who could do all tasks without depending on the use of some type of corrective lenses (e.g. glasses or contacts) to prevent insufficient infrared reflection during the eyetracking paradigm (Antisaccade task). Participants provided written informed consent before testing and either received course credit or monetary compensation for their participation. The study protocol was approved by the Ethics committee of the University of Bamberg.

2.2. Procedure

Upon arriving at the laboratory, participants were told that the experiment was designed to investigate the relationship between pain and inhibition. Participants were further told that this would be realized by assessing self-reported pain intensity, eye-movements via EMG- and video-recording and the performance in inhibitory tasks. Thus, by reducing the emphasis on our interest in facial expressions, the participants' focus on their facial expressions was supposed to be attenuated.

The experiment consisted of two blocks. During the first block the degree of facial expressiveness was assessed (facial expressiveness block). This was done by applying a set of painful and non-painful thermal stimuli and recording the degree of facial expressiveness in response to these stimuli via video and electromyography (EMG). In the second block of the experiment the ability to inhibit was determined (inhibitory functioning block). This was realized by conducting the Antisaccade task (testing motor inhibition), the Stroop task (testing behavioral and cognitive inhibition) and the German version of the UPPS Impulsive behavior scale (testing impulse control via self-report).

2.3. Facial expressiveness block

2.3.1. Pain induction

Following a previous protocol that has been shown to successfully elicit facial responses to pain (Kunz et al., 2011; Kunz, Scharmann, Hemmeter, Schepelmann, & Lautenbacher, 2007), thermal stimulation was applied on the tibia of the left leg (centrally in between knee and ankle) by a Peltier based contact stimulation device (Medoc, TSA-2001, Ramat Yishai, Israel) with a 30 mm × 30 mm contact thermode. To ensure that all participants perceived the pre-set stimuli as similarly painful during the assessment of facial expressiveness, temperature intensities were tailored

to the individual pain threshold. As a result of this, it was guaranteed that individual differences in the degree of facial expressiveness were not simply due to differences in perceived pain intensity. Heat pain thresholds were therefore determined first, using the method of adjustment. Participants were asked to adjust a temperature starting from 38 °C, using heating and cooling buttons, until they obtained a level which was barely painful. A constant press of the buttons produced a heating or cooling rate of 0.5 °C/s. Following a familiarization trial, there were 4 trials and the average of these trials was used to constitute the threshold estimate.

Following the assessment of pain thresholds, the intensities for the two types of stimuli were determined: non-painful (−1 °C below the pain threshold) and painful stimulation (+3 °C above the pain threshold). Participants received ten painful and ten non-painful stimuli in a random order. Applying also non-painful intensities allows a determination of the degree to which facial responses during thermal stimulation are indeed specific for painful experiences. Due to individual differences in pain threshold, target temperatures varied between 41.3 °C and 47.7 °C for non-painful stimuli and between 45.3 °C and 51.0 °C for painful stimuli. Each phasic heat stimulus (painful/non-painful) had the same characteristics (5 s (plateau); rate of change: 4 °C/s; baseline temperature: 38 °C; inter-stimulus-intervals of 15–20 s). The trapeze-shaped stimuli, thus, consisted of a phase with temperature rise (variable length between .83 s and 3.25 s – depending on the type of stimulus (painful/non-painful) and individual target temperature), 5 s of constant target temperature and a decrease of temperature toward baseline (same duration as the phase of rise). Following each stimulus, perceived pain intensity was assessed using self-report ratings. This was realized by using a visual analog scale (VAS; 100 mm) on an electronic shift register, which was placed on the table in front of the participants. Participants were told that the left and right ends of the scale corresponded to "no sensation" and to "extremely strong pain", respectively. In addition, the scale was labeled with a verbal anchor of "faintly painful" in the center so that all non-painful sensations should be rated to the left and all painful ones to the right of the center. Participants were instructed to rate the intensity of their pain by matching their perceived pain intensity with a certain distance on the scale. This was achieved by moving the cursor (which was set to the middle of the scale before each trial) to the right or left.

2.3.2. Degree of facial expressiveness (criterion variable)

2.3.2.1. Facial Action Coding System (FACS). The face of the participants was videotaped throughout the pain induction procedures. The camera was located approximately 3.0 m from the participant. In order to mark the plateau phase of the stimuli, a LED visible to the camera, but not to the participant, was lit concurrently with the 5 s-thermal stimulation, starting when the target temperature was reached. During stimulation, participants were instructed not to talk and to look at an emotionally neutral painting on the wall behind the camera to ensure that the face would always be recorded in an upright and frontal view.

Facial expressions were coded from the video recordings using the Facial Action Coding System (FACS; Ekman & Friesen, 1978), which is based on anatomical analysis of facial movements and distinguishes 44 different Action Units (AUs) produced by single muscles or combinations of muscles. One of the authors, a certified FACS coder (qualified by passing an examination given by the developers of the system) identified the frequency and the intensity (5-point scale) of the different Action Units. To guarantee reliability of the coding, another certified FACS coder re-coded 10% of the data; with an interrater reliability of .86 as calculated using the Ekman–Friesen formula (Ekman & Friesen, 1978). A software designed for the analysis of observational data (the Observer Video-Pro; Noldus Information Technology) was used to segment the videos and to enter the FACS codes into a time-related database. Time segments of 7 s beginning just after stimulus had reached the target temperature were selected for scoring. In total, 20 segments of thermal stimulation (10 non-painful and 10 painful segments) were analyzed in each subject. For the purpose of necessary data reduction, we combined similar facial responses as has been done in preceding studies without any loss of information (Hale & Hadjistavropoulos, 1997; Karmann et al., 2014; Kunz, Mylius, Schepelmann, & Lautenbacher, 2004; Kunz et al., 2007; Prkachin, 1992). Those combinations include AU 1/2, AU 6/7, AU 9/10 and AU 25/26/27.

Pain-relevant AUs were selected based on the procedure developed in previous studies (e.g. Kunz, Mylius, Schepelmann, & Lautenbacher, 2008; Kunz et al., 2007) using the following steps: (1) AUs had to occur in more than 5% of the painful segments recorded and (2) AUs had to be more frequent during painful than during non-painful trials (effect size $d \geq 0.5$; these AUs are marked in bold in Table 1). This chosen subset of pain-relevant AUs is consistent with previous findings regarding facial responses to pain (Craig et al., 2011; Karmann et al., 2014; Kunz et al., 2008) and consists of the following AUs: AU 4 (lowering of the brows), AU 6/7 (orbit tightening) and AU 9/10 (levator contraction). Following, mean AU-frequency and mean AU-intensity values of the selected AUs were combined (product terms) and averaged across all selected AUs to form a *composite score* of pain-relevant facial responses. Due to the fact that these composite scores were not distributed normally (Kolmogorov–Smirnov $Z = 1.545$, $p < .05$), *square root transformed composite scores* were used for further analyses as has also been done in previous studies (Karmann et al., 2014; Kunz et al., 2011; Kunz, Faltermeier, & Lautenbacher, 2012).

2.3.2.2. Electromyographic (EMG) recording and analysis. Facial surface EMG was recorded over the region of orbicularis oculi (one of the most activated muscles in the response to pain; Prkachin, 1992) below the left eye using two Ag/AgCl electrodes filled with electrode paste. The electrodes were placed according to the guidelines for standard electrode placement by Fridlund and Cacioppo (1986). Prior to application of the electrodes, skin was cleaned with an alcoholic skin detergent to reduce electrode resistance. The acquisition of EMG raw signal was carried out by the device SIGMA Plpro/Type Databox DB 36 including a 16 bit AD-convertor with a dynamic range from 0.5 μV to 2 mV. The recording bandwidth of the EMG signal was between 0.2 Hz and 300 Hz; input resistance was above 20 mOhm. The signal was sampled at 512 Hz.

Analysis of the raw EMG signal was done offline by the program "Vision Analyzer" (Brain Products, Munich). In the first step, the signal was cut into 7-s segments which contained the EMG response starting when the stimulus had reached the target temperature (painful/non-painful). The signal of each segment was subsequently filtered (50 Hz notch filter, 20 Hz high-pass filter, 250 Hz low-pass filter), rectified and integrated (100-ms time constant). Following, a sum-score was calculated for the signal of the 7-s period creating a score that covered the same time period as the FACS score. For baseline correction, the trials with non-painful stimulation (reference situation; Hess, 2012) were considered. The EMG data of each subject was thus z-transformed across painful and non-painful trials.

When comparing the two measures of facial expressiveness, one notices that the EMG measure reflected the activity of a single muscle (orbicularis oculi) whereas the FACS measure was less regionally specific and can potentially include all facial movements. Despite this difference, these two measures were chosen for the following reason. The EMG signal – as a measure with high intensity resolution – might even be adequate when only using a single recording site with particular relevance for the facial expression of pain. A single Action Unit (AU) of the FACS on the other hand might not be as sensitive given that one single muscle movement does not become visible in every trial. Furthermore, the chosen composite score has been shown to be a more valid measure of the facial response to pain than any single AU (Prkachin & Solomon, 2008). The better sensitivity of the FACS composite score compared to the single AU covering orbicularis oculi activity (AU 6/7) can also be seen when correlating the two measures with the EMG score (see Section 3.1).

Table 1
Facial action units (AUs) with a critical frequency of occurrence of more than 5% in painful segments.

Action Unit	Percent[a]	Effect size
AU 1/2	7.8	0.25
AU 4	26.2	**0.59**
AU 6/7	44.3	**0.88**
AU 9/10	9.8	**1.07**
AU 12	5.5	0.38
AU 14	9.8	0.21
AU 17	7.1	0.14
AU 25/26/27	14.7	0.49

Effect sizes for frequency differences between "non-painful" and "painful" segments are given. Medium and strong effect sizes ($d \geq 0.5$) are marked in bold.

[a] Percent denotes the percentage of occurrence in the entire painful segments.

2.4. Inhibitory functioning block (assessment of predictor variables)

2.4.1. The Antisaccade task

To assess the ability to inhibit an automatic motor response, we conducted the Antisaccade task by replicating the experimental set-up of Derakshan, et al. (Derakshan, Ansari, Hansard, Shoker, & Eysenck, 2009). Stimulus presentation and tracking of eye movements were conducted by a system distributed by the company Interactive Minds, Dresden. This system consisted of a 19 inch Samsung LCD-screen (resolution 1280 × 1024 pixels; 60 cm viewing distance) and the eyetracking system Eyegaze Edge™ by LC Technologies Inc and was driven by the software NYAN 2XT (version 2.3.3). In order to measure the pupil's orientation, this eyetracking system uses the corneal reflection of an infrared light source (corneal reflex method; Mason, 1969). It features a sampling rate of 60 Hz and a fidelity of 0.4°.

Each trial began with the presentation of a fixation cross (12 mm × 12 mm, 1.15° × 1.15°) in the center of the screen which was to be fixated until it disappeared (2000 ms). In addition, two dark gray rectangular frames were presented left and right of the fixation cross (60 mm × 60 mm, 5.73° × 5.73°; located at 8.29° horizontally from the fixation cross) to indicate the destination of the later saccade. These two frames were then constantly present in all following images. Next, a circle (diameter = 35 mm, 3.34°) which represented the "cue" appeared for 600 ms. The cue was either presented within in the frame in the left or right side of the screen (11° horizontally from the fixation cross) with both locations being equally probable. Depending on the instruction given at the beginning of each block, participants were asked to look either toward the cue (Prosaccade block) or away from it (Antisaccade block), as quickly as possible. Afterwards, an arrow pointing up or down (11 mm × 24 mm, 1.05° × 2.29°), which served as "target" was presented for 100 ms. The target either appeared in the same location as the cue (Prosaccade block) or on the opposite side of the screen (Antisaccade block). The participants had to identify the direction of the arrow via pressing the up or down key of a regular computer

keyboard, as fast and accurate as possible. This approach served the purpose of maintaining the participant's vigilance and given that our main focus lay on the inhibition of automatic occulomotor reactions, key-press reaction time data was not further analyzed. The task consisted of six blocks (three Prosaccade and three Antisaccade blocks; alternating), with 12 trials each, which resulted in a total of 72 trials. One half of the participants started the test with a Prosaccade block, the other half with an Antisaccade block. Ahead of testing, participants practiced the task in a short training block consisting of 8 trials.

The measures chosen for further analyses were – based on previous work (Derakshan et al., 2009) – the following: *Latency of the first correct saccade* (latency of the first saccade (time interval between cue onset and start of the first fixation) in the right direction) and *percentage of incorrect saccades* (percentage of first saccades in the wrong direction). Inhibitory functioning was then determined by calculating the differences between Anti- and Pro-saccade trials for the two variables *(in the following called* Δ). High scores, resulting from big differences between Anti- and Prosaccade trials, thus indicated a poor ability to inhibit (inhibitory functioning), whereas low scores indicated a high degree of inhibitory functioning.

2.4.2. The Stroop task

In order to additionally assess a variable which is hypothetically more distantly related to facial expressiveness, the Stroop task (Stroop, 1935) was conducted. For this purpose, a computerized version of the Stroop task was created with E-Prime Version 2.0. There were four blocks consisting of the classical stroop conditions. In two of the blocks the presented color word ("red", "green", "blue" or "yellow") had to be named; once in a neutral condition where the color word was printed in black (word naming – neutral; WN_{neu}) and once when the color words were incongruently colored in one of the other three colors (word naming – incongruent; WN_{incg}). In the other two blocks the color of the stimulus had to be named; once again in a neutral condition where the stimuli consisted of a row of x's (XXXXX) that were presented in either red, green, blue or yellow (color naming – neutral; CN_{neu}) and once when the color words were again incongruently colored in one of the other three colors (color naming – incongruent; CN_{incg}). The order of the blocks was randomized across participants. All stimuli were presented centrally on a 19 inch EIZO LCD-screen (resolution 1280 × 1024 pixels; 60 cm viewing distance) in Arial, font size 30. Instructions explaining the task appeared on the screen ahead of each block. Each stimulus was presented until the subject responded. All responses were given via one of four color-labeled keys on a regular computer keyboard ("L", "P", "R", "G"; located within a range of 12 cm) using the index finger of the dominant hand. As indicators of inhibitory functioning, scores for the *stroop-effect* (reaction time of CN_{incg}–CN_{neu}) and the *reverse stroop-effect* (reaction times of WN_{incg}–WN_{neu}) were calculated neglecting erroneous trials. Again, high scores indicated a low degree of inhibitory functioning whereas low scores indicated a high degree of inhibitory functioning.

2.4.3. Self-evaluation of impulse control

In order to assess the self-evaluation of impulse control, we used the UPPS Impulsive Behavior Scale (Whiteside & Lynam, 2001) which was developed to measure four dimensions of impulsive behavior, namely *Urgency*, *Lack of Premeditation*, *Lack of Perseverance* and *Sensation Seeking*. The inventory contains 45 items that are rated on a four-point scale with the end points "agree strongly" and "disagree strongly". The UPPS has been widely used in research and the German version has been shown to be a robust and valid measure for impulsive behavior (Kämpfe & Mitte, 2009; Schmidt, Gay, d'Acremont, & van der Linden, 2008).

2.5. Statistical analysis

First, descriptive statistics (Mean, standard deviation) were calculated for the Antisaccade and Stroop task, as well as the UPPS. In order to demonstrate that inhibition prevailed, *t*-tests for independent samples were further calculated to determine whether variables differed between the Anti- and Prosaccade blocks and for the *stroop* and *reverse stroop effect*. In order to screen for multicollinearity (in the following regression analyses), Pearson's correlations were additionally conducted for relationships amongst and between the criteria (facial expressiveness) and predictor variables (inhibitory functioning).

To test our main hypotheses, sequential multiple regression analyses were conducted in order to find out whether inhibitory functioning can predict the degree of facial expressiveness. For this purpose the measures of inhibitory functioning were entered into the analysis block wise. The order of entrance was thereby determined by the relevance of the measure; starting with the least and ending with the most relevant. This way the more relevant measures of inhibitory functioning were evaluated for their additional predictive value after controlling for variations explained by less relevant variables (conservative approach). Accordingly, the model consisted of the following blocks: The UPPS variables (*Urgency*, *Lack of Premeditation*, *Lack of Perseverance* and *Sensation Seeking*) were entered in the first block, the Stroop task variables (*stroop effect*, *reverse stroop effect*) in the second and the Antisaccade task variables (Δ *latency of the first correct saccade*, Δ *percentage of incorrect saccades*) in the third block. In order to assess the association of inhibitory functioning and facial expressiveness measured by FACS as well as EMG, two separate regression analyses were conducted. In one of them, the FACS-composite score served as criterion, while in the other one the EMG-signal of orbicularis oculi was used.

Given that directed hypotheses existed, one-way tests were conducted for the main (regression) analyses. For all analyses, findings were considered to be statistically significant at $\alpha < 0.05$.

3. Results

In the present study the mean pain threshold amounted to 46.0 °C (SD = 1.55). Participants on average rated the painful stimulation (+3 °C above threshold) clearly above 50 (M = 80.8; SD = 9.6) whereas the non-painful stimulation (−1 °C below threshold) was on average rated as clearly below 50 (M = 18.1; SD = 13.2) on the VAS. The ratings of the two stimulus intensities differed significantly from each other ($t(48) = 32.0$; $p < .001$). Descriptive data of the predictor variables is given in Table 2. As expected, the *latency of the first correct saccade* and the *percentage of incorrect saccades* in the Antisaccade task were significantly higher in the Antisaccade compared to the Prosaccade trials ($t(48) = 17.98$; $t(48) = 8.72$; all $p < .001$). With regard to the Stroop task, the present data showed a *stroop effect*, as well as the *reverse stroop effect*; with the reaction times of color naming – incongruent (CN_{incg}) trials being significantly longer than those of color naming – neutral (CN_{neu}) trials ($t(48) = 5.71$; $p < .001$) and the reaction times of word naming – incongruent (WN_{incg}) trials being significantly longer than those of word naming – neutral (WN_{neu}) trials ($t(48) = 9.79$; $p < .001$). The findings of the present study were, thus, within normal limits and the proper use of the tests, indicating inhibitory functioning, can be assumed.

3.1. Intercorrelations (within criteria and predictor variables)

Facial measurements (*criteria*): Although the EMG recording was only assessed over the orbicularis oculi muscle, we did not want to restrict the FACS criterion to the activity of orbicularis oculi, but rather use a score which represents the activity of all pain-relevant muscles in the face and, thus, used the composite score (including AU 4, AU 6/7, AU 9/10) as the FACS criterion variable. As can be seen in Table 3, FACS composite score of the whole face and EMG recording of the orbicularis oculi muscle were strongly correlated ($r = .702$; $p < .001$).[1]

Measures of Inhibitory functioning (*predictors*): As can be seen in detail in Table 3, the UPPS variables were correlated so that Lack of Premeditation was significantly related to Urgency, as well as Sensation Seeking. The UPPS variable Lack of Perseverance was significantly related to both Antisaccade measures; the Δ *latency of the first correct saccade* as well as the Δ *percentage of incorrect saccades*. Besides that, none of the UPPS variables were significantly related to each other or any of the Antisaccade or Stroop variables (all $p > .05$). Surprisingly, the Stroop measures were neither significantly related to each other nor to the Antisaccade measures (all $p > .05$). The Antisaccade variables Δ *latency of the first correct saccade* and Δ *percentage of incorrect saccades* were significantly related to each other. Thus, none of the predictors correlated highly with predictors from the other predictor groups.

3.2. Prediction of the degree of facial expressiveness by inhibitory functioning

3.2.1. FACS composite score as criterion

As illustrated in Table 4, the sequential multiple regression revealed that the UPPS (β-weights ranging between –.01 and .15)

[1] Moderate to strong correlations between FACS and EMG were also found when AU 6/7 was excluded from the composite score ($r = .696$; $p < .001$), as well as when the single unit score of AU 6/7 (which should cover the same muscle movements as the EMG recording) was used ($r = .572$; $p < .001$).

Table 2
Descriptive results for the different predictor categories with mean values and standard deviations (measures used for regression analysis printed in bold).

Category	Measure	Mean	SD	*t*	*p*
Anti-saccade task	Latency of first correct saccade – pro	250 ms	32.6	Anti vs. Pro	
	Latency of first correct saccade – anti	379 ms	45.0	17.98	<.001
	Antisaccade – Δ Latency correct (=latency of first correct saccade (anti-pro))	129 ms	50.1		
	Percentage of incorrect saccades – pro	8.16%	7.0	Anti vs. Pro	
	Percentage of incorrect saccades – anti	25.25%	15.0	8.72	<.001
	Antisaccade – Δ Percentage incorrect (=percentage of incorrect saccades (anti-pro))	17.10%	13.7		
Stroop	CN_{neu}	915 ms	112.8	CN_{neu} vs. CN_{incg}	
	CN_{incg}	1083 ms	242.9	5.71	<.001
	Stroop effect	169 ms	206.8		
	WN_{neu}	951 ms	151.2	WN_{neu} vs. WN_{incg}	
	WN_{incg}	1227 ms	248.8	9.79	<.001
	Reverse stroop effect	276 ms	197.5		
UPPS	**Urgency**	27.06	5.18		
	Lack of Premeditation	24.08	4.28		
	Lack of Perseverance	19.65	3.99		
	Sensation Seeking	34.78	6.73		

CN_{neu} = color naming (non-word stimulus); CN_{incg} = color naming of incongruently colored color-words; WN_{neu} = word naming of black color-words; WN_{incg} = word naming of incongruently colored color-words; UPPS = Impulsive Behavior Scale.

could not significantly contribute to explaining the variations in facial expressiveness measured by FACS. Entering the Stroop variables (β-weights ranging between −.21 and .12) into the model did also not add significantly to explaining the variations in facial expressiveness. Not until the Antisaccade variables were entered into the model (see Table 4), the predictive value of the model changed significantly ($\Delta R^2 = .183$; $p < .01$). It showed that the Antisaccade variables (*Δ latency of the first correct saccade, Δ percentage of incorrect saccades*) were positively related to the FACS composite score (β weights ranging between .08 and .11). Thus, the lower the level of inhibition was during the Antisaccade task (indicated by higher Δ-values), the stronger the participants expressed their pain via the face.

3.2.2. EMG-activity as criterion

When using the orbicularis oculi EMG-activity as measure of facial expressiveness, similar results evolved (see Table 4). Again, neither the UPPS (β-weights ranging between −.06 and .19) nor the Stroop task variables (β-weights ranging between −.19 and .02) could significantly contribute to explaining the variations in facial expressiveness. However, entering the Antisaccade variables (see Table 4) changed the predictive value of the model significantly ($\Delta R^2 = .119$; $p < .05$). It showed that the Antisaccade variables (*Δ latency of the first correct saccade, Δ percentage of incorrect saccades*) were again positively related to the EMG activity of orbicularis oculi (β-weights ranging between .11 and .33). Thus, the lower inhibitory functioning was in the Antisaccade task (indicated by higher Δ-values), the more expressive were the individuals.

As can be seen in Sections 3.2.1 and 3.2.2, the same pattern of significant and non-significant associations was found when FACS composite scores or EMG activity of orbicularis oculi were used as measures of facial expressiveness (criteria). Whether the two criterion variables can statistically substitute each other, however, cannot be drawn from these results. In order to test the mutual substitutability, we conducted partial correlations eliminating either the influence of EMG or FACS when correlating the performance in the Antisaccade task with FACS or EMG, respectively. In order to avoid multiple testing (due to multiple Antisaccade parameters), the performance in the Antisaccade task was in this context represented by the sum of the z-standardized Antisaccade parameters (which was possible since both parameters acted in the same direction and were highly correlated). The results show that the correlation of the performance in the Antisaccade task and the FACS score ($r = .380$, $p < .01$) does not remain significant when controlling for the EMG score ($r = .195$, $p = .184$). Likewise, the significant correlation between the performance in the Antisaccade task and the EMG score ($r = .356$, $p < .05$) disappears when controlling for the FACS score ($r = .136$, $p = .357$). These findings indicate that FACS and EMG can indeed statistically substitute each other in the present study.

4. Discussion

The main purpose of the present study was to investigate whether the degree to which individuals facially express their inner affective state, namely pain, can be predicted by different aspects of inhibitory functioning. As expected, we found a strong negative relationship between motor inhibitory functioning assessed by the Antisaccade task and facial activity during painful stimulation (measured via FACS and EMG). The stronger the inhibitory control of motor responses was, the weaker an individual expressed his/her pain via the face. In contrast, the degree of facial expressiveness did neither depend on the inhibitory performance in the Stroop task nor on impulse control assessed by the UPPS. These findings will be discussed in detail below.

Although research on facial expressions of pain has had a long history, to date still little is known about the mechanisms regulating the degree of facial expressiveness. Our results now suggest that the degree of facial expressiveness during pain is related to the ability to inhibit automatic motor responses. More precisely, we found that the degree of facial expressiveness could be predicted by the performance in the Antisaccade task. Individuals who perform well in this task are highly able to inhibit the automatic orientation saccade toward an abruptly appearing peripheral stimulus. Interestingly, the stronger this ability was pronounced, the less facially expressive individuals were when experiencing moderately painful heat. These results seem to be well in line with the results of recent brain imaging findings investigating cerebral activation patterns during the facial expression of pain (Kunz et al., 2011) and disgust (Goldin, McRae, Ramel, & Gross, 2008). Both studies showed concordantly that areas known to be involved in motor inhibition – such as the medial prefrontal cortex and the basalganglia – were more active when facial expressiveness was low. Thus, combining these findings with our current results strongly suggests that

Table 3
Pearson's correlations between predictor and criterion variables (r (+p-values)) significant results are marked in bold.

		Orbicularis occuli EMG activity	Antisaccade – Δ Latency correct	Antisaccade – Δ% incorrect	Stroop effect	Reverse stroop effect	Urgency	Lack of premeditation	Lack of perseverance	Sensation seeking
Criteria	FACS composite score	**.702 (<.001)**	**.394 (.005)**	**.311 (.029)**	−.170 (.243)	.112 (.445)	.107 (.462)	.184 (.207)	.171 (.241)	.057 (.696)
	Orbicularis occuli EMG activity		**.291 (.043)**	**.371 (.009)**	−.168 (.250)	.040 (.783)	.147 (.312)	.147 (.312)	.161 (.269)	.148 (.312)
Predictors	Antisaccade – Δ Latency correct			**.723 (<.001)**	.043 (.768)	.004 (.976)	.220 (.128)	−.116 (.426)	**.348 (.014)**	−.077 (.600)
	Antisaccade – Δ% incorrect				−.115 (.433)	−.006 (.970)	.274 (.057)	−.137 (.349)	**.383 (.007)**	−.052 (.724)
	Stroop effect					−.019 (.895)	−.086 (.556)	.091 (.536)	.109 (.457)	.085 (.562)
	Reverse stroop effect						.212 (.144)	.055 (.706)	−.037 (.802)	.041 (.781)
	Urgency[a]							**.415 (.003)**	.261 (.070)	.260 (.072)
	Lack of Premeditation								.235 (.104)	**.438 (.002)**
	Lack of Perseverance									−.007 (.963)

[a] The obtained pattern of intercorrelations between the UPPS subscales is similar to previous findings Whiteside and Lynam (2001),Whiteside, Lynam, Miller, and Reynolds (2005); Miller, Flory, Lynam, and Leukefeld (2003).

Table 4
Linear regression models for FACS composite score (criterion) and orbicularis occuli EMG activity (criterion). Predictors in step 1: *Urgency, Lack of Premeditation, Lack Perseverance and Sensation Seeking* (UPPS); added predictors in step 2: *stroop effect, reverse stroop effect* (Stroop task); added predictors in step 3: Δ *Latency of the first correct saccade*, Δ *percentage of incorrect saccades* (Antisaccade task); significant results are marked in bold.

Step	Variables added	Total R^2	ΔR^2	p (for Δ in R^2)
FACS composite score				
1	+ UPPS	.051	.051	.335
2	+ Stroop	.104	.053	.150
3	+ Antisaccade	.287	.183	**.005**
Orbicularis occuli EMG activity				
1	+ UPPS	.061	.061	.294
2	+ Stroop	.096	.035	.223
3	+ Antisaccade	.215	.119	**.030**

inhibitory mechanisms seem to play a crucial role in the (down-)regulation of facial expressiveness – at least when considering the expression of negative affective states such as pain and disgust.

The robustness of our findings is supported by the fact that the relationship between facial expressiveness and the performance in the Antisaccade task was found when using FACS scores as well as EMG activity as measures of facial expressiveness. This result is even more intriguing when considering the differences of the two measures. On the one hand, FACS quantifies visible muscle movements in the face, whereas the EMG signal reflects slight changes in muscular activity, which are not necessarily visible. Secondly, with FACS the activity of all muscles in the face was coded while the EMG signal was only derived from orbicularis oculi; single site recording was necessary to not interfere with facial expressiveness. Although orbicularis oculi – as one of the most active muscles in the response to pain (Prkachin, 1992) – represents the best possible single parameter of the facial response to pain, recording its activity can never cover all aspects of the facial pain response. Nevertheless, even when only represented by the EMG activity of one muscle, facial expressiveness of pain could be predicted by the Antisaccade task. The association between the ability to inhibit automatic motor responses and facial expressiveness, thus, seems to be robust independent of the measure of facial expressiveness.

In contrast to the Antisaccade task, the performance in the Stroop task could not contribute significantly to explaining variance in the degree of facial expressiveness. Methodological shortcomings cannot account for this difference given that we found the usual *stroop* as well as the *reverse stroop effect* with sufficient strength (cf. Miyake et al., 2000). It thus can be assumed that the Stroop task was performed according to the state-of-the-art. Therefore, it is more likely that the Stroop and the Antisaccade task target different types of inhibitory functioning; which are differently related to the processes involved in the regulation of facial expressiveness. The Antisaccade task requires the inhibition of a reflex saccade (Hutton & Ettinger, 2006) while the Stroop task engages the inhibition of a discriminative operant (non-reflex) response based on semantic information processing (Nigg, 2000). Thus, two clearly distinguishable types of inhibition seem to be targeted which is also suggested by the lack of correlation between the Antisaccade und Stroop variables. Facial expressions are motor responses which can be both reflex and voluntary in nature (Craig et al., 2011). It can be assumed that facial responses to noxious stimuli in a socially deprived environment – as our experimental laboratory – are better explained by a reflex mechanism. Accordingly, it seems likely that the performance in the Antisaccade task (inhibition of a reflex saccade) and the degree of facial expressiveness were both regulated by similar reflex mechanisms and filtered through the same "inhibitory gate". The performance in the Stroop task on the other hand might be regulated by another "inhibitory gate" given that higher cognitive processes are demanded in this

case. Thus, especially inhibitory motor control seems to be crucial for the (down-)regulation of facial expressiveness.

This assumption is corroborated by brain imaging findings. Brain activation during the Antisaccade task shows close resemblance to the activation involved in the regulation of facial expressiveness, overlapping e.g. in the prefrontal cortex and the basalganglia (Ford, Goltz, Brown, & Everling, 2005; Goldin et al., 2008; Kunz et al., 2011; Munoz & Everling, 2004). In contrast, inhibitory performance in the Stroop task was mainly associated with the activation of anterior cingulate cortex (ACC), insula, premotor and inferior frontal areas (Leung, Skudlarski, Gatenby, Peterson, & Gore, 2000), which were not found to be active during the inhibition of facial expressiveness (Goldin et al., 2008; Kunz et al., 2011).

The context, in which this close relationship between inhibitory motor control and facial expressiveness applies, however, might be limited. As mentioned before, facial expressions can also be characterized as voluntary. This is the case in socially enriched situations, where the voluntary programming of facial activity can become more relevant (e.g. social/affiliative smiling; Niedenthal, Mermillod, Maringer, & Hess, 2010). Here, the consequences of expressing inner affective states have to be considered and the reflex response can be overridden e.g. when individuals try to fake or aggravate facial expressions (Craig et al., 2011; Hadjistavropoulos et al., 2011). In such contexts, it seems less likely that the inhibitory regulation of reflex activity has the same relevance in determining the degree of facial expressiveness. In order to be able to quantify the impact of reflex and voluntary inhibitory regulation mechanisms, further studies including socially enriched contexts are, thus, necessary.

Our analyses did not indicate a significant association between self-evaluated impulse control (UPPS) and the degree of facial expressiveness. This was both the case for the FACS- as well as the EMG-scores. How can this be explained? On the one hand, the different measures might have accessed different levels of processing. The completion of self-report measures such as the UPPS rather demands the subject's explicit and conscious processing (Kline, 2000), whereas the degree of facial expressiveness measured by objective, implicit measures (FACS; EMG) is not instructed to be monitored while it is assessed. On the other hand, there might just simply be no association. Even though both, impulse control (Gay et al., 2008; Roberts et al., 2011) and facial expressiveness (current study) have been shown to be associated with inhibitory functioning, the two do not necessarily have to be related. It, thus, seems possible that impulsive behavior and facial expressiveness are regulated by different inhibitory mechanisms.

4.1. Limitations

A limitation of the present study might be that we only tested facial expressiveness during painful stimulation. Our results now indicate that certain aspects of inhibitory functioning can predict the degree of facial expressiveness in response to pain whereas others cannot. Whether this pattern of significant and non-significant associations can also be found for other affective states has to be demonstrated in further studies.

4.2. Summary

Our findings clearly indicate that the degree of facial expressiveness in response to pain can be predicted by the ability to inhibit automatic motor responses (Antisaccade task). Accordingly, the better an individual is able to inhibit automatic motor responses, the less facially expressive he/she seems to be. In contrast, there does not seem to be a similar relationship between inhibitory functioning demanding cognitive processing (Stroop task) or self-evaluated impulse control (UPPS) and facial expressiveness. These results suggest that the degree of facial expressiveness in response to pain is specifically regulated by motor inhibitory mechanisms, but is not regulated by inhibitory mechanisms in general.

This association applies to situations, in which the facial activity is triggered by preceding pain stimuli and has little instrumental relevance for social interactions, in other words where facial activity is rather of reflex nature. Such situations are prevalent, comprising most of the everyday acute pains. However, it is still an open question whether the inhibition of automatic motor responses plays a similarly critical role when facial activity during negative affective states is more instrumental, aiming at social impact and reward.

Disclosures

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Anhang 2: Studie II

Karmann, A. J., Maihöfner, C., Lautenbacher, S., Sperling, W., Kunz, M. (…). The role of prefrontal inhibition in regulating facial expressions of pain: a rTMS study.

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The role of prefrontal inhibition in regulating facial expressions of pain: a rTMS study

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Abstract

Although research on facial expressions of pain has had a long history, little is known about the cerebral mechanisms regulating these expressions. Recent imaging data suggests that the medial prefrontal cortex (mPFC) might be involved in regulating/inhibiting the degree to which pain is displayed via the face. The current study was conducted to test whether such a prefrontal regulation does indeed take place by reducing the prefrontal cortical excitability via repetitive transcranial magnetic stimulation (rTMS) and assessing its effect on facial expressions.

In a within-subject design, facial and subjective responses to pressure and heat pain were assessed in 35 healthy participants; once after receiving 20 minutes of low-frequency rTMS over the mPFC (1Hz; 1200 impulses) and once after sham stimulation was applied.

Compared to sham stimulation, low-frequency rTMS over the mPFC resulted in enhanced facial expressions of pain. This effect was shown for both types of painful stimuli (pressure, heat). Self-report ratings of pain intensity did, in contrast, not differ between rTMS and sham stimulation.

The current data demonstrate that reducing prefrontal excitability leads to enhanced facial expressions of pain. This finding indicates that prefrontal areas are crucially involved in the inhibition of facial expressions of pain. The fact that this effect was independent of changes in self-report ratings suggests that this inhibitory mechanism is mainly governing the facial expression and does not seem to alter the underlying experience of pain.

1. Introduction

Although research on facial expressions of pain even dates back to Darwin [10], little is yet known about the cerebral mechanisms regulating these expressions. Recent studies have now postulated that inhibitory mechanisms might play a role in this context. More specifically, the degree to which individuals show their pain via the face seems to depend on the amount of motor inhibition that an individual exerts over his/her facial expression [26]. As has been revealed by an imaging study of our group [28], this inhibitory regulation of the facial expression of pain might be guided by medial prefrontal regions. Thus, the activation of fronto-striatal networks including medial prefrontal cortex (mPFC) was shown to be higher when individuals facially displayed their pain to a lesser extent and vice versa [28]. These results were in line with earlier findings which also reported an increased activation of prefrontal areas when healthy participants were instructed to actively inhibit facial expressions while watching negative emotion-eliciting films [21].

Although showing coherent and plausible results, these previous findings cannot verify that medial prefrontal activation necessarily results in an inhibition of facial expressions of pain. The proposed association, however, can be tested by using a technique that has been developed in recent years: repetitive transcranial magnetic stimulation (rTMS). Via repeated application of magnetic pulses on the skull, the neural activity of defined brain regions can be decreased or even disrupted by low-frequency rTMS (≤ 1Hz); which has been shown for different areas of the brain (motor [7,18,37] and visual cortex [5]). During this rTMS-induced period of attenuated excitability, it is then possible to assess the function of the targeted cortex regions [47].

The main goal of the present study was to make use of this technique (rTMS) in a sham-controlled design to examine whether facial expressions of pain can be altered by changing prefrontal excitability. If medial prefrontal activation was indeed crucial for the exertion of inhibitory control over the facial expression of pain, facial expressions in response to painful stimulation should be stronger during the period of lower prefrontal excitability (due to 1Hz-rTMS) compared to sham stimulation.

Based on the previous findings [28], mPFC served as the starting point. For this purpose the rTMS coil was centered over FPz (according to the 10/20 system [1]). This has been done in previous studies [4,22] and should – with a rTMS-reach of 1.5 – 2 cm beneath the scalp [15,44] – ensure stimulation of mPFC. Low-frequency rTMS was here chosen over high-frequency rTMS (> 1Hz), which would have increased prefrontal excitability. The resulting further increase of inhibition might have lowered the facial expression of pain under the limit of detection and out of reach of reasonable assessment.

In order to exclude that potential rTMS-induced changes in facial expressions were due to changes in pain perception itself, we compared self-report ratings between rTMS and sham stimulation. Furthermore, it was tested whether rTMS-induced changes in subjective and facial responses were correlated. Given that rTMS over mPFC is – in contrast to rTMS over dorsolateral prefrontal and motor cortex – not known to alter pain ratings (for a review see [39]), we did, however, not expect rating differences between rTMS and sham stimulation.

2. Materials and Methods

2.1 Participants

The 36 participants (20 females; M = 25.6 years; SD = 9.7) were recruited by bulletins put up throughout the campus of the University of Bamberg. Before the first session, psychology research assistants conducted a structured telephone screening with each participant in order to gather necessary information on the participant's health status. In this process, individuals with chronic pain, psychological, neurological or physical illnesses or those taking psychotropic drugs or analgesics were excluded from participation. All of the participants were further free of any contraindications to rTMS (e.g. seizures, cardiac pacemakers; for a detailed description see [47]) and pain-free during the experimental sessions. Participants provided informed written consent before testing and received monetary compensation for their participation. The study protocol was approved by the Ethics committee of the Medical School of the University of Erlangen-Nuremberg.

2.2 Procedure

The experiment consisted of three procedurally almost identical sessions. The first session took place in a laboratory at the University of Bamberg (training session) and the following two testing sessions were held at the Department of Psychiatry of the University Hospital of Erlangen (rTMS/sham session) (see Fig. 1a). During the session in Bamberg, participants first filled out questionnaires covering different personality variables. As stated above, this appointment in Bamberg also served as a training session. Accordingly, participants underwent the same experimental procedures (with the same equipment) that were to take place in the following two sessions in Erlangen. This way, participants became accustomed to the experimental protocol and instructions could be shortened during the following testing sessions (rTMS/sham). The resulting time-efficiency in the testing sessions was important given that rTMS effects are limited to a short period of time [12,43]. Given that the session in Bamberg primarily served as a training session, the data collected here were not entered into the final analyses comparing rTMS and sham effects.

In the two testing sessions in Erlangen, each participant once received rTMS and once sham stimulation (within-subject design). The order of stimulation was pseudo-randomized (50% starting with rTMS, 50% starting with sham) by also taking into account that the proportion of female and male participants who first received rTMS or sham stimulation was balanced. In order to prevent rTMS carry-over effects, there was at least one week in between the two sessions. Each session started with either rTMS or sham stimulation, directly followed by the assessment of facial expressions during painful stimulation. This was done by applying a set of (i) painful and non-painful mechanical stimuli as well as (ii) painful thermal stimuli while recording facial expressions. Mechanical Stimuli were always applied first, followed by thermal stimulation. This order was chosen in order to avoid carry-over effects of subsequently presented stimuli which would be more likely when the more sustained thermal stimulation (≥10s) would precede the short-term pressure stimulation (5s) [34].

2.3 Repetitive transcranial magnetic stimulation (rTMS)

Magnetic stimulation was applied by a Dantec MagPro MC 125 stimulator, using a figure-8-shaped coil with dynamic fluid cooling, which was attached to an adjustable arm. During stimulation participants were seated in a comfortable chair that was adjusted so that their upper body was in an almost horizontal, supine position. This approach was chosen to ensure a good positioning of the rTMS coil above the mPFC. In order to stimulate the mPFC, the coil was centered at the location of FPz in the 10/20 system [1] as has also been done in previous studies [4,22]. In each session, participants received 20 minutes of biphasic stimulation consisting of 1200 impulses with a rate of 1Hz. rTMS was adjusted to 90% of the individual motor-cortex threshold. The motor cortex threshold was determined by applying single pulses with increasing intensities over the left precentral gyrus (M1) until movement of the right thenar was detected optically. For sham stimulation, a sham coil that resembled the active one in color, shape and size and emitted similar sounds, but did not actually emit magnetic pulses, was similarly positioned over mPFC. This type of

sham stimulation was chosen over other methods of effect control to ensure an unaltered activity of the target site during the sham condition. When using control-site stimulation, potential long-range effects of rTMS [17] prevent the exclusion of stimulation effects at the target site. This is similar in tilted sham conditions which have also been shown to always cause some degree of active stimulation [35,36].

All participants were blinded to the condition of the respective session. They knew that in only one of the sessions an active treatment (rTMS) would be applied, but did not know which session that was. In order to assess whether the stimulation caused any type of discomfort (e.g. headache), participants were asked about their well-being right after the stimulation. This question was posed after rTMS as well as sham stimulation with the purpose of keeping a standardized protocol during both sessions. One of the participants reported having a headache after (rTMS-)stimulation and was, thus, excluded from further participation.

2.4 Facial expressions of pain

2.4.1 Pain induction

In order to assess the generalizability of rTMS effects on facial expressions across different pain induction methods, two different types of painful stimulation were applied. First, we chose short-term pressure stimuli (5s) which cause both superficial and deep tissue nociception [2] of a relatively small body area. Second, sustained heat stimulation (10s) – realized by hand immersion in painful hot water – was chosen to elicit superficial tissue nociception over a relatively large body area. We, thus, applied two of the most commonly used physical stressors that differed with regard to the nociceptors being targeted, the amount of spatial summation involved and the length of stimulation. Despite these differences, both stimulation types were supposed to elicit moderate pain intensities. This was ensured by inspecting the self-report data acquired in the training session. Pressure stimulation was always applied first, followed by thermal stimuli. In both cases the order of stimulation sides (left/right) was balanced across participants.

2.4.1.1 Pressure Stimuli

Pressure stimuli were delivered by experienced investigators using a handheld pressure algometer (Algometer type II, Somadic Sales AB, Hörby, Sweden) with an implemented indicator of the rate of rise and a probe area of 1 cm^2. Sites of stimulation were the left as well as the right volar forearm (distal to proximal) and the shoulder (over the head of the trapezius muscle). Steady support was guaranteed by placing the participants arm on the armrest of the chair and in case of shoulder stimulation – which was applied from above – by an upright seating position and instructions telling the participants not to move away from stimulation. For each stimulation site, two different stimulus intensities were applied (see Fig. 1b), namely a painful (500kPa) as well as a non-painful (200kPa) intensity (oriented towards norms for pressure pain thresholds (see [16,38,40])). Applying non-painful intensities allows a comparison of facial expressions between painful and non-painful stimulations and, thus, a determination of which types of facial responses are indeed specific for painful experiences (see 2.4.2). The pressure was steadily increased from 0 kPa at a rate of rise of 100 kPa/s until the defined stimulus intensity had been reached. The pressure was then continued at that level for another 5 s. The interval between stimulus applications varied between 10 and 20 s. Participants received four painful (one on each of the two shoulders, one on each of the two forearms) and four non-painful stimuli (one on each of the two shoulders, one on each of the two forearms) in a pseudo-randomized order.

Following each stimulus, participants had to verbally rate their pain intensity using a numerical rating scale (NRS; 0-100) on which “0” corresponded to “no pain” and “100” to “extremely strong pain”. They were asked to name the number that best matched their perceived pain intensity.

2.4.1.2 Heat Stimuli

Heat stimuli were applied using two circulation water baths (Witeg GmbH, WiseCircu WCB-22, Wertheim, Germany) containing water at a temperature of either 35°C (baseline)

or 47.5°C (painful). A baseline temperature was applied in order to be able to compare facial expressions between baseline and painful stimulation and, thus, determine which types of facial responses are indeed specific for painful experiences (see 2.4.2). The participant immersed her/his hand up to 2 cm above the wrist in these water baths. Water temperature was controlled with a thermostat, and the water was stirred with a force and suction pump to avoid layers of lower temperature around the hand. Heat stimuli were applied to the right as well as to the left hand (randomized order across participants). Stimulation started with participants immersing one hand in the 35°C water (see Fig. 1b). After 30 seconds, participants immersed the same hand in the 47.5°C water for three times (the first time for 10 s, then for 15 s and then for 20 s). The inter-stimulus intervals, during which the hand was again immersed in the (baseline) 35°C water, were 30 seconds long. An extension of the immersion time in the painful water bath during the second and third trial was necessary to keep the perceived pain intensity levels equal (as assessed in the training session: mean NRS for $1^{st}/2^{nd}/3^{rd}$ immersion trials were 63.9 / 63.5 / 64.8). After a short pause, this procedure was then repeated with the other hand.

Following each painful stimulus, participants had to verbally rate their pain intensity using the same NRS as when rating pressure stimuli. Again “0” corresponded to “no pain” and “100” to “extremely strong pain”. They were asked to name the number that best matched their perceived pain intensity (providing an overall judgement for the full length of the stimulus). The 35°C baseline temperature was not rated.

2.4.2 Measurement of facial expressions

The face of the participants was videotaped throughout the pain induction procedures. The camera was located approximately 2.0 m from the participant. A LED visible to the camera, but not to the participant, was lit concurrently with the stimuli to mark the onset of stimulation. To ensure that the face would always be upright, steady and in a frontal view during stimulation, participants were asked to look forward and – apart from rating the stimuli – not to talk during stimulation.

Facial expressions were coded from the video recordings using the Facial Action Coding System [14], which is based on anatomical analysis of facial movements and distinguishes 44 different Action Units (AUs) produced by single muscles or combinations of muscles. Two of the authors, blind to the treatment (rTMS or sham), identified the frequency and the intensity (5-point scale) of the different Action Units. Both coders were qualified by passing an examination given by the developers of the FACS and the interrater reliability mounted up to .82 as calculated using the Ekman–Friesen formula [14]. A software designed for the analysis of observational data (the Observer Video-Pro; Noldus Information Technology) was used to segment the videos and to enter the FACS codes into a time-related database. Depending on the type of stimulation (pressure or heat), different time segments were chosen to be coded (see Fig. 1b). In the case of pressure stimuli, 7 s segments (5 s covering the time that target pressure was applied + 2 s) were selected for scoring. When analyzing heat stimuli, 12 s segments (10 s at the end of each painful stimulus/each baseline period + 2 s) were coded. The reason for coding the 2 s after the end of stimulation was that facial expressions often persist beyond stimulus offset. In total, 8 segments of mechanical stimulation (4 painful and 4 non-painful segments) and 12 segments of thermal stimulation (6 painful and 6 baseline segments) were analyzed for each participant in each session (rTMS/sham). For the purpose of necessary data reduction, we combined those AUs that represent similar facial movements as has been done in preceding studies without any loss of information [23,25,27,29,41]. Those combinations include AU1/2, AU6/7, AU9/10 and AU25/26/27.

In order to determine which of the AUs are pain-relevant, we used a procedure developed in previous studies (e.g. [27,32]) consisting of the following steps: (a) AUs had to occur in 5% of the painful pressure segments and in 10% (due to longer stimulation times) of the painful heat segments recorded, and (b) AUs had to be more frequent during painful than during non-painful segments (pressure) or baseline segments (heat), respectively (effect size $d \geq 0.5$; these AUs are marked in bold in Table 1). Interestingly, more AUs fulfilled these criteria after rTMS compared to sham stimulation (additional two AUs for both

pressure and heat stimulation; cf. Table 1). However, in order to create scores that enabled a comparison between the strength of the facial expressions in the sham and rTMS condition, only those AUs fulfilling criteria (a) and (b) for both conditions (sham, rTMS) were chosen for further proceeding. The resulting subsets of pain-relevant AUs (shaded in grey in Table 1) are consistent with previous findings regarding the facial expression of pain [8,25,27].

Next, mean AU-frequency and mean AU-intensity values of the selected AUs were combined (product terms) and averaged across all selected AUs to form a *composite score* of pain-relevant facial expressions (cf. [25,27,31]). Composite scores were separately calculated for each method of pain induction (pressure/heat) and each treatment condition (Sham/rTMS). Following the same procedure, but using the scores of all AUs that did not prove to be pain-relevant, we also computed *composite scores* of pain-irrelevant facial expressions. This was done to enable a determination of whether rTMS-treatment led to an unspecific increase in facial expressions or whether it only increased facial expressions of pain.

Due to the fact that most of the composite scores were not distributed normally (Kolmogorov-Smirnov Zs ranging between 1.26 and 2.0, all $p < .085$), square root transformed composite scores were used for further analyses as has also been done in previous studies [25,29,31].

2.5 Statistical analysis

Analyses only focused on facial and subjective responses during painful stimulation. Given that non-painful pressure and 35°C baseline temperature were only applied to provide a “baseline-reference” needed to determine pain-relevant and pain-irrelevant responses, they were not considered.

Step 1: rTMS-effects on facial expressions

In order to assess the impact of low-frequency rTMS on facial expressions during painful stimulation, the following analyses were conducted. The FACS composite scores of facial

expressions (see section 2.4.2) were submitted to analyses of variance (ANOVA) with repeated measures (within-subject factors: treatment (sham, rTMS) and category of facial expression (pain-relevant, pain-irrelevant)). Two separate ANOVAs were conducted for facial expressions elicited by pressure and by heat pain.

Step 2: rTMS-effects on self-report ratings

In a second step, we wanted to find out whether the applied rTMS had an effect on self-report ratings of painful stimuli. Thus, ANOVAs with repeated measures (within-subject factor: treatment (sham, rTMS)) were performed with self-report ratings of pain intensity (NRS) for pressure and heat pain as dependent variables.

Results for the within-factor analyses were corrected according to Greenhouse–Geisser whenever the Mauchly-test of sphericity indicated heterogeneity of covariance. In case of significant effects in the univariate analyses, post-hoc t-tests were calculated.

Step 3: Relationship between changes in facial expressions and changes in self-report ratings induced by rTMS

In a last step, we wanted to determine whether the rTMS-induced changes in pain-relevant facial expressions were correlated with changes in self-report ratings. For this purpose, change scores between rTMS and sham stimulation (rTMS – sham) were calculated for both, changes in facial expressions and changes in self-report ratings. Following, these change scores were entered into bivariate correlation analyses for both types of painful stimuli (pressure, heat).

In case of significant correlations, the analyses described in Step 1 would be rerun with the changes in pain ratings entered as covariates. This served the purpose to exclude that rTMS-induced changes in facial expressions are due to changes in perceived pain intensity.

Findings were considered to be statistically significant at $\alpha<0.05$. Besides p-values, we also report partial eta-squared (η_p^2) as a measure of effect size.

3. Results

When being asked which stimulation type was applied (rTMS or sham), 66.7% of the participants could not name the correct stimulation type in the first session and in the second session still 33.3% of the participants answered incorrectly. Furthermore, the probability of determining the correct stimulation was in both cases not significantly different from chance level (all $p > .05$). Consequently, we were successful in blinding participants with regard to the type of treatment they received.

Step 1: rTMS-effects on facial expressions

As illustrated in Figure 2, pain-relevant composite scores differed strongly from pain-irrelevant composite scores during painful stimulation, which was the case during pressure ($F(1,34) = 34.996$, $p<.001$, $\eta =.507$) as well as during heat stimulation ($F(1,34) = 40.106$, $p<.001$, $\eta =.541$). As expected, pain-relevant composite scores were higher than pain-irrelevant composite scores (see Figure 2) after both, sham stimulation and rTMS ($t=[-6.123;-4.988]$; all $p<.001$).

With regard to our main hypothesis, we found a significant difference in FACS composite scores between rTMS and sham stimulation. Again, this effect was present during pressure ($F(1,34) = 13.853$, $p<.005$, $\eta =.289$) and heat stimulation ($F(1,34) = 9.369$, $p<.005$, $\eta =.216$) with similarly strong effect sizes. As shown in Figure 2, participants were facially more expressive during painful stimulation after rTMS compared to sham stimulation. Post-hoc testing showed that rTMS elevated pain-relevant as well as pain-irrelevant composite scores ($t=[-3.806;-2.591]$; all $p<.05$). However, a strong interaction between category of facial expression and treatment indicated that this effect differed between pain-relevant and pain-irrelevant composite scores. This interaction was found

for both, pressure ($F(1,34) = 14.945$, $p<.001$, $\eta =.305$) and heat stimulation ($F(1,34) = 4.683$, $p<.05$, $\eta =.121$). As can be seen in Figure 2, pain-relevant composites scores were – compared to pain-irrelevant composite scores – more strongly elevated due to rTMS. Furthermore, when calculating difference scores between pain-relevant and pain-irrelevant composite scores, it became apparent that the differences between these two scores were significantly increased after rTMS compared to sham stimulation (all $p<.05$).

Step 2: rTMS-effects on self-report ratings

Figure 3 shows how the self-report ratings as provided by the NRS were affected by the different treatment options. As opposed to FACS composite scores, self-report ratings did not differ between rTMS and sham stimulation, which was the case for pressure ($F(1,34)=2.136$, $p=.153$, $\eta=.059$) as well as for heat stimuli ($F(1,34)=.000$, $p=.994$, $\eta=.000$).

Step 3: Relationship between changes in facial expressions and changes in self-report ratings induced by rTMS

Despite rTMS and sham stimulation having no different effect on self-report ratings, it is possible that rTMS-induced changes in facial expressions covary with similar changes in pain intensity ratings. This can be seen in Figure 4 which shows that changes (differences between rTMS and sham) in pain-relevant FACS composite scores correlated positively with changes in pain intensity ratings. This was the case for both, pressure ($r=.327$, $p<.05$ one-sided) and heat stimuli ($r=.407$, $p<.01$ one-sided). Thus, although self-report of pain was not overall affected by rTMS, the more facial expressions were enhanced after rTMS, the more intense did participants rate the pain stimuli.

This correlation could, however, also indicate that the changes in facial expressions might partly be due to changes in pain intensity ratings caused by rTMS. To exclude this possibility, the analyses described in Step 1 were rerun with the changes in pain intensity ratings as covariates. This measure did, however, not change the results. For pressure as

well as heat stimuli, there were still similar sized main effects of “category of facial expression” (pressure ($F(1,34) = 30.857$, $p<.001$, $\eta =.483$); heat ($F(1,34)= 41.076$, $p<.001$, $\eta=.555$)) and “treatment” (pressure ($F(1,34) = 10.701$; $p <.005$, $\eta=.245$); heat ($F(1,34) = 10.674$; $p <.005$, $\eta=.244$)). The interaction between “category of facial expression” and “treatment” was also still present with similar effect sizes (pressure ($F(1,34) = 12.190$, $p<.005$, $\eta =.270$); heat ($F(1,34) = 5.466$, $p<.05$, $\eta =.142$). Thus, even when partialling out the influence of rTMS-induced changes in pain intensity ratings, rTMS significantly affected facial expressions during painful stimulation.

4. Discussion

The present study was designed to investigate whether the facial expression of pain can be altered by changing medial prefrontal excitability via rTMS. Indeed, low-frequency rTMS over mPFC, which should induce a reduction of prefrontal excitability, resulted in enhanced facial expressions of pain. This pattern emerged for two types of painful stimulation (pressure, heat). A reduction of prefrontal excitability further seems to mainly affect facial expressions while the subjective experience remains unaltered, given that rTMS did not affect self-report ratings of pain intensity. When correlating changes in facial and subjective responses induced by rTMS, however, a significant positive relationship was found. Subsequent analyses of covariance nonetheless showed that rTMS-induced effects on facial expression could not be explained by changes in self-report ratings. These findings will be discussed in detail below.

Even though research on the facial expression of pain has been conducted for decades, only very recently it was shown what mechanism might underlie the regulation of these expressions. In line with earlier findings on the facial display of disgust [21], our group [28] could previously demonstrate that reduced facial expressions of pain were associated with the activation of medial prefrontal cortex. Given that this area is known to be involved in

motor inhibition [3,42], it was hypothesized that reduced facial expressions of pain might be due to an active prefrontal inhibition. On a behavioral level this hypothesis could be corroborated by finding an association between the inhibition of automatic, motor responses (Antisaccade Task) and the degree to which individuals show their pain via the face [26]. It was, however, to be shown that a change in prefrontal activation would indeed result in an inhibition of facial expressions of pain. The current study was, thus, conducted to test the proposed association by applying low-frequency rTMS over the mPFC which was – based on previous research – the most promising target. It is known that low-frequency rTMS in the range that we used (1Hz) induces a decrease in cortical excitability [7,18,37]. Hence, in the period right after rTMS, the potential influence of the targeted prefrontal areas should be reduced due to their lower activity. During this period, we found facial expressions of pain to be enhanced compared to sham stimulation. This was reflected in higher composite scores as well as a higher amount of AUs occurring during painful stimulation after rTMS. Reducing prefrontal activation by rTMS, thus, seemed to have decreased inhibitory control over facial expressions which led to a “release” of the overt facial display of painful experiences. Together with our previous results [26,28], this finding strongly supports the assumption that inhibitory mechanisms play a major role in regulating the facial expression of pain and that medial prefrontal areas exert this inhibitory control.

This interpretation also seems to be in line with developmental observations. The ability to express certain emotions via the face is thought to be innate to a high degree [13]. During the first months, facial expressions are seen as rather stimulus driven and reflexive [9]. Throughout development children then gradually learn to control and adjust their facial expressions according to social rules [24,45]. This is accompanied by a maturation of prefrontal areas, which continues from early childhood up to late adolescence [19,20]. Thus, the maturation of prefrontal areas might facilitate or promote the development of a control of facial expressions. The fact that this acquired control is usually associated with a decrease in facial expressions (at least with regard to the expression of negative

affective states) [24] further favors the idea of a learnt active inhibition of facial expressions.

The generalizability of the present finding is indicated by the fact that facial expressions in response to painful heat and pressure stimuli were equally influenced by low-frequency rTMS. Thus, rTMS over the mPFC resulted in a stronger display of the painful experience in both cases. The effect was hence evident, independent of whether facial expressions were elicited by short-term deep tissue nociception involving little spatial summation (pressure stimuli) or more sustained superficial nociception involving a high amount of spatial summation (heat stimuli). Accordingly, the inhibitory activity of the prefrontal cortex seems to generally regulate facial expressions in response to pain independent of the eliciting pain stimulus.

Low-frequency rTMS application over the mPFC also seemed to affect both categories of facial expressions. Thus, both, pain-relevant as well as pain-irrelevant facial expressions were enhanced after rTMS-treatment. A significant interaction between category of facial expression and treatment, however, indicated that this effect was differently pronounced for the two categories of facial expressions. The application of rTMS over the mPFC, thus, resulted in a significantly higher elevation of pain-relevant compared to pain-irrelevant facial expressions and an enhanced difference between the two categories of facial expression. Accordingly, the prefrontal inhibitory mechanism investigated here should be considered fairly specific, given that its primary focus seems to be the “signal” (pain-relevant facial expressions) of facial pain communication. Although also influencing the “noise” (pain-irrelevant facial expressions) (which might be facilitated by enhanced pain-relevant facial expressions), it seems to affect the signal-noise distance in a way that the “signal” is more emphasized. The detected mechanism, thus, seems to specifically target the communicative strength of the facial expression of pain rather than just adapt the general level of facial muscle activity.

The here outlined prefrontal inhibitory mechanism should, however, by no means be seen as the only mechanism regulating the facial expression of pain. The afore mentioned fMRI study [28] also detected an association between the strength of facial pain expressions and the activity of primary motor cortex as well as areas involved in the processing of pain (primary somatosensory area, insula and anterior cingulate cortex). Given that in this case a positive correlation arose, the activity of these areas might be responsible for inducing an internal drive to express pain via the face. Thus, at least two mechanisms controlling the facial expression of pain seem to exist: (1) An internal drive to express pain via the face and (2) an inhibitory outlet control of the generated facial expression.

Finding that pain intensity ratings were – in contrast to facial expressions – unaffected by the rTMS-induced reduction of prefrontal activity further corroborates this idea and specifies the interaction between the two mechanisms. The selective modulation of prefrontal activity, thus, changed one output of the pain experience (facial expression) whereas it left another (self-report) unaltered. This indicates that prefrontal activity does not exert control over facial expressions by down-regulating the pain experience and, thus, the internal drive to facially express pain itself, but rather by controlling the outlet of the internally called and generated facial expressions.

Even though no systematic differences in pain ratings occurred between rTMS and sham stimulation, we found a significant positive relationship between changes in subjective and facial responses induced by rTMS. This finding could be due to two reasons. On the one hand – as just discussed above – it is known that facial expressions increase with increasing perceived pain intensity [8,30]. Hence, the rTMS-induced enhancement of facial expressions could have been due to increases in pain intensity. This possibility is, however, very unlikely, given that even when partialling out the influence of rTMS-induced changes in pain ratings, a significant rTMS-effect on facial expressions could be detected. Another reason for the detected association might be that rTMS-induced changes in facial expressions affected the experience of pain. This interpretation would be in line with the

predictions of the facial feedback hypothesis (FFH). This hypothesis states that a strong facial display of emotions causes an enhancement of the emotional experience whereas an inhibition of facial expressions weakens the experience [6,11,33,46].

Limitations

One limitation of the present study – as in most previous studies using rTMS in the context of pain research – might be that a double-blind design was not established and the experimenter was thus aware of the treatment (rTMS or sham) applied in each of the sessions. In order to reduce a possibly resulting bias, the interaction between participant and experimenter was limited to a minimum and followed a standardized protocol which was identical in all sessions.

Conclusion

The present study shows that a reduction of medial prefrontal excitability induced by low-frequency rTMS causes an enhancement of facial expressions of pain. This finding strongly supports the assumption that medial prefrontal activation is causally involved in the inhibition of the facial expression of pain. The fact that this effect was independent of changes in the subjective pain experience further suggests that this outlet control mechanisms runs largely independent from the activity of pain-generating areas in the brain.

Disclosures

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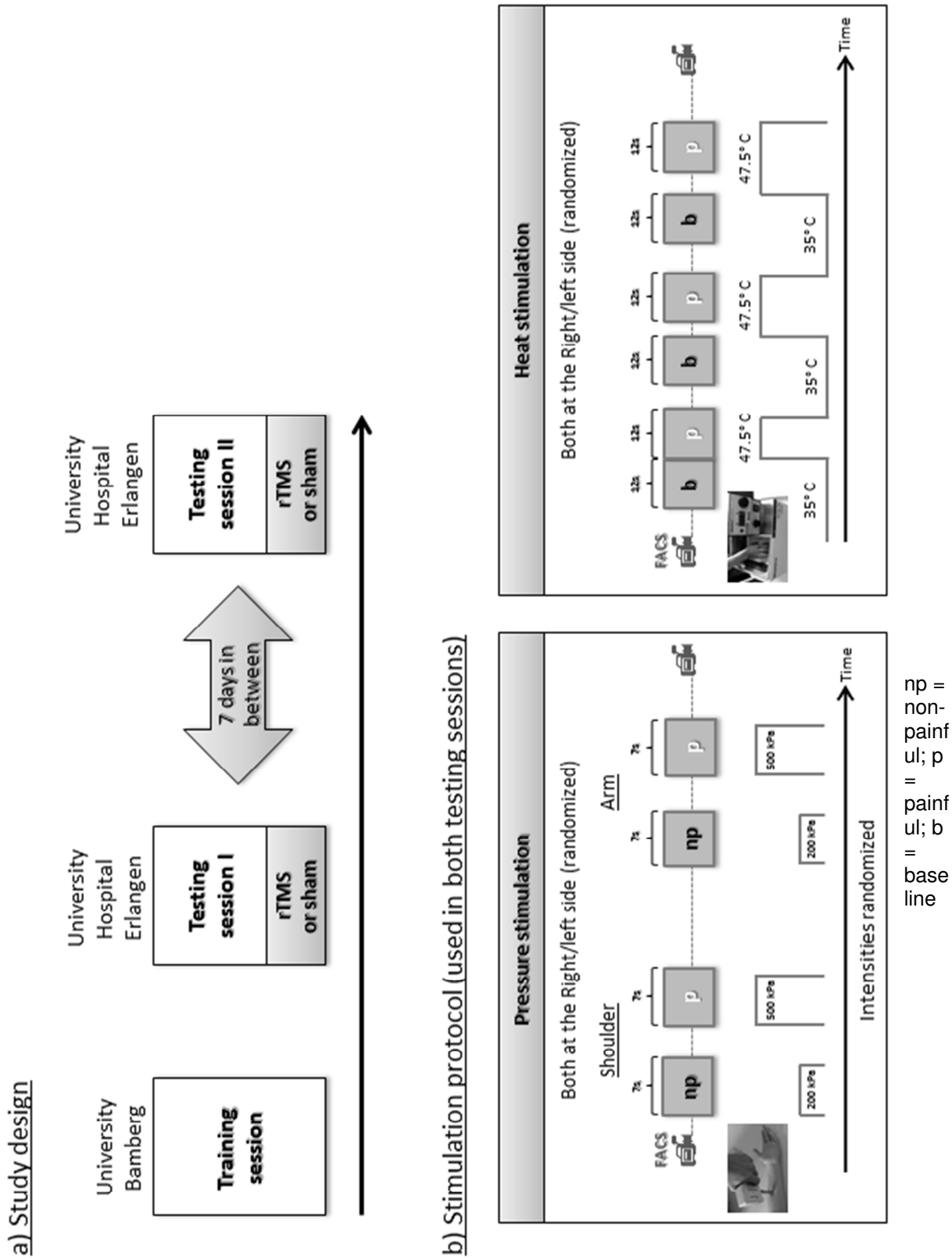
Table 1: Facial Action Units (AUs) with a critical frequency of occurrence of more than 5% in all painful segments (pressure and heat stimulation presented separately). Data are presented for Sham and rTMS.

	Pressure				**Heat**			
	Sham		**rTMS**		**Sham**		**rTMS**	
Action Unit	Percent[a]	Effect size	Percent[a]	Effect size	Percent[a]	Effect size	Percent[a]	Effect size
AU 1/2	11.8	0.3	24.3	**0.6**	21.4	**0.5**	25.7	**0.6**
AU 4	27.1	**0.7**	44.4	**1.4**	26.2	**0.6**	41.0	**0.8**
AU6/7	56.3	**1.0**	85.4	**1.1**	54.8	**0.9**	94.8	**1.0**
AU 9/10	22.9	**0.6**	53.5	**1.0**	20.5	**0.6**	31.4	**0.5**
AU 12	5.6	0.3	11.1	**0.8**	6.0	0.2	8.1	0.4
AU 14	9.0	0.3	17.4	**0.7**	29.5	0.3	39.0	**0.9**
AU 15	(1.4)	-	(2.1)	-	(3.8)	-	5.2	0.3
AU 17	(2.1)	-	8.3	0.1	11.0	0.4	12.9	0.4
AU 18	(2.1)	-	(2.1)	-	(4.3)	-	8.6	0.3
AU19	(0)	-	(0)	-	(2.4)	-	6.7	0.1
AU 24	(4.9)	-	5.6	0.4	11.4	0.2	11.9	0.4
AU 25/26	13.9	**0.5**	24.3	**0.5**	39.0	0.4	55.2	**0.6**
AU 28	(2.8)	-	(2.1)	-	10.0	0.2	11.4	0.2
AU 43	9.7	**0.6**	12.5	**0.7**	7.6	0.4	11.0	0.3

Effect sizes for frequency differences between ‘‘non-painful/baseline” and ‘‘painful” segments are given. Medium and strong effect sizes (d ≥ 0.5) are marked in bold. AUs included in the composite score are shaded in grey.
[a] Percent denotes the percentage of occurrence in the entire painful segments.

Figures

Figure 1: Study design (a) and stimulation protocol (b)



np = non-painful; p = painful; b = baseline

Figure 2: Mean values (+SD) for FACS composite scores (sqrt transformed) of evoked facial expressions in response to painful stimulation. Values are given separately for pain-relevant and pain-irrelevant facial expressions, the two treatment options (Sham, rTMS) as well as the two types of stimulation (pressure, heat).

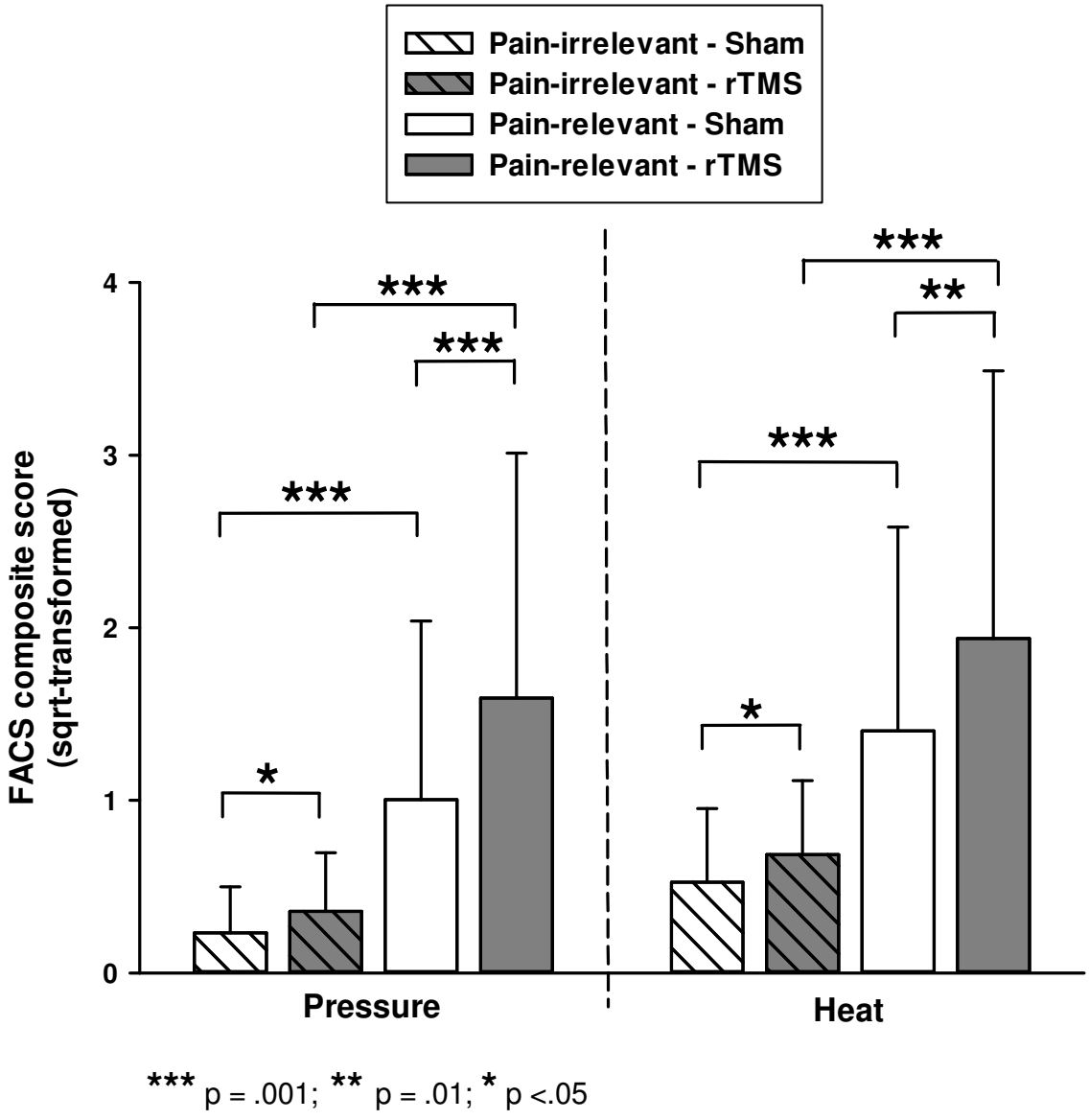


Figure 3: Mean values (+SD) for self-reported pain intensity assessed by a numerical rating scale (NRS). Values are given separately for the two types of stimulation (pressure, heat) and the two treatment options (Sham, rTMS).

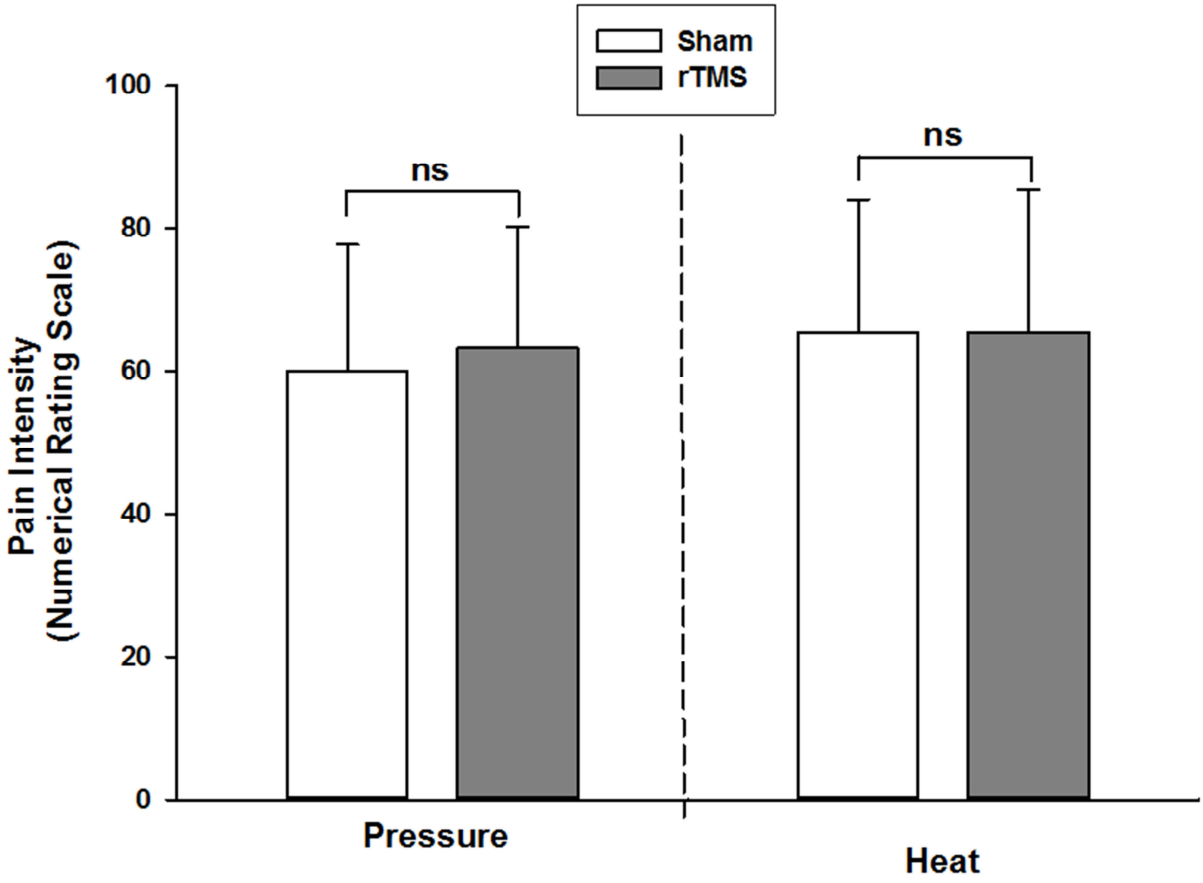
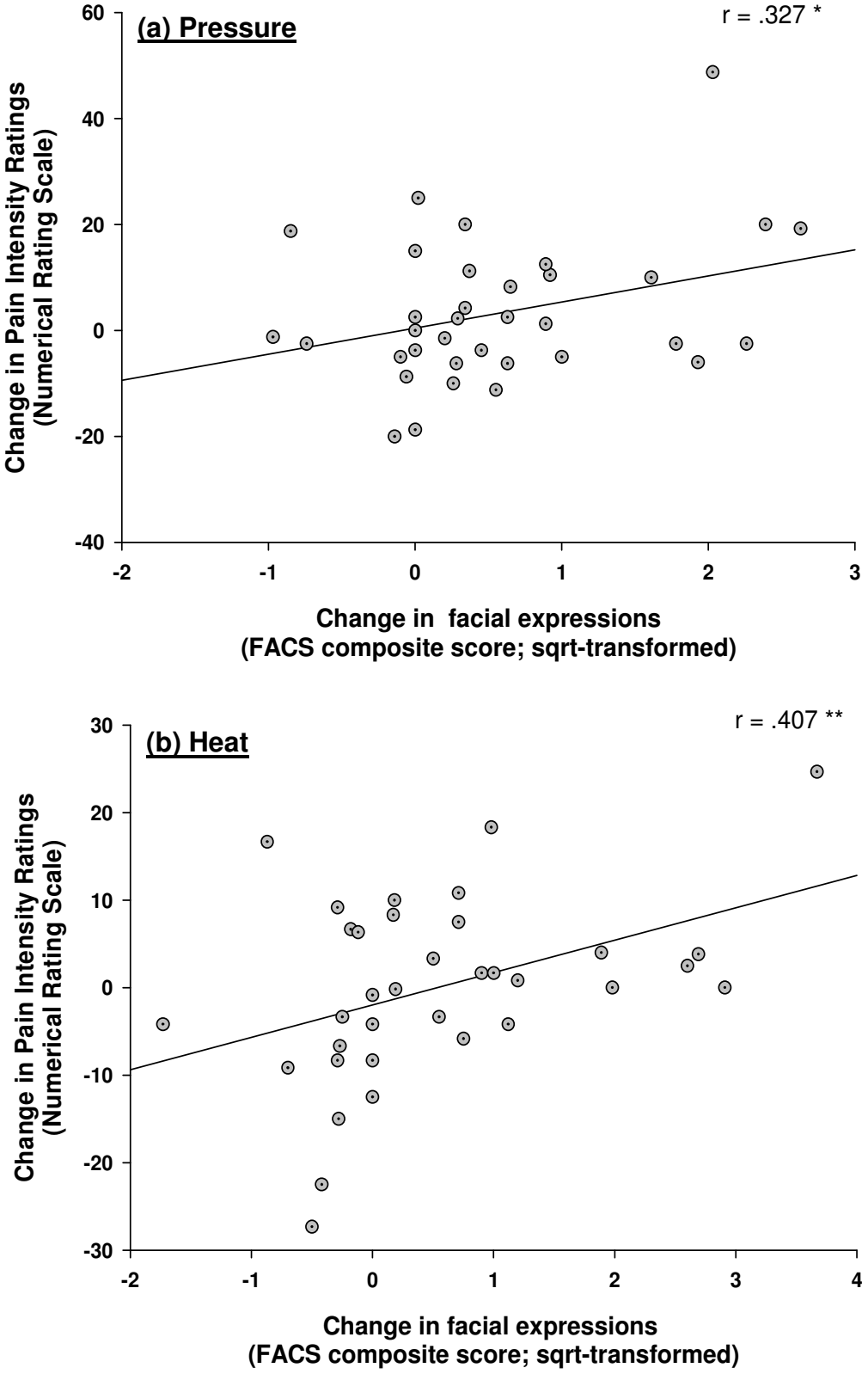


Figure 4: Bivariate correlations between changes (difference between rTMS and sham stimulation) in pain-relevant FACS composite scores and self-reported pain intensity for (a) painful pressure stimuli and (b) painful heat stimuli.



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Anhang 3: Studie III

Karmann, A. J., Lautenbacher, S., Bauer, F., Kunz, M. (2014). The influence of communicative relations on facial responses to pain: does it matter who is watching? *Pain Research & Management* 19 (1), S. 15–22.

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ORIGINAL ARTICLE

The influence of communicative relations on facial responses to pain: Does it matter who is watching?

Anna J Karmann MSc, Stefan Lautenbacher PhD, Florian Bauer MSc, Miriam Kunz PhD

AJ Karmann, S Lautenbacher, F Bauer, M Kunz. The influence of communicative relations on facial responses to pain: Does it matter who is watching? Pain Res Manag 2014;19(1):15-22.

BACKGROUND: Facial responses to pain are believed to be an act of communication and, as such, are likely to be affected by the relationship between sender and receiver.
OBJECTIVES: To investigate this effect by examining the impact that variations in communicative relations (from being alone to being with an intimate other) have on the elements of the facial language used to communicate pain (types of facial responses), and on the degree of facial expressiveness.
METHODS: Facial responses of 126 healthy participants to phasic heat pain were assessed in three different social situations: alone, but aware of video recording; in the presence of an experimenter; and in the presence of an intimate other. Furthermore, pain catastrophizing and sex (of participant and experimenter) were considered as additional influences.
RESULTS: Whereas similar types of facial responses were elicited independent of the relationship between sender and observer, the degree of facial expressiveness varied significantly, with increased expressiveness occurring in the presence of the partner. Interestingly, being with an experimenter decreased facial expressiveness only in women. Pain catastrophizing and the sex of the experimenter exhibited no substantial influence on facial responses.
CONCLUSION: Variations in communicative relations had no effect on the elements of the facial pain language. The degree of facial expressiveness, however, was adapted to the relationship between sender and observer. Individuals suppressed their facial communication of pain toward unfamiliar persons, whereas they overtly displayed it in the presence of an intimate other. Furthermore, when confronted with an unfamiliar person, different situational demands appeared to apply for both sexes.

Key Words: *Communicative relations; Facial expression; FACS; Pain; Social variations*

L'influence des relations de communication sur les réponses faciales à la douleur : l'observateur a-t-il une importance?

HISTORIQUE : On pense que les réponses faciales à la douleur sont un acte de communication. À ce titre, la relation entre l'émetteur et le récepteur est susceptible de les influencer.
OBJECTIFS : Examiner les conséquences des variations des relations de communication (être seul ou avec un proche) sur les éléments du langage facial utilisé pour communiquer la douleur (types de réponses faciales) et sur le degré d'expression faciale.
MÉTHODOLOGIE : Les chercheurs ont évalué les réponses faciales de 126 participants en santé à une douleur phasique causée par la chaleur dans trois situations sociales différentes : seul, mais conscient d'un enregistrement vidéo en cours, en présence d'un expérimentateur et en présence d'un proche. De plus, la catastrophisation de la douleur et le sexe (du participant et de l'expérimentateur) étaient considérés comme des influences supplémentaires.
RÉSULTATS : Les chercheurs ont observé des types de réponses faciales similaires quelle que soit la relation entre l'émetteur et l'observateur, mais le degré d'expression faciale variait considérablement et atteignaient un paroxysme en présence du conjoint. Fait intéressant, la présence d'un expérimentateur réduisait l'expression faciale seulement chez les femmes. La catastrophisation de la douleur et le sexe de l'expérimentateur n'avaient aucune influence importante sur les réponses faciales.
CONCLUSION : Les variations des relations de communication n'ont pas d'effet sur les éléments du langage facial de la douleur. Le degré d'expression faciale est toutefois adapté à la relation entre l'émetteur et le récepteur. Les individus suppriment leur communication faciale de la douleur devant des personnes non familières, mais l'expriment ouvertement en présence d'un proche. De plus, devant une personne non familière, diverses exigences situationnelles semblent entrer en jeu chez les deux sexes.

Communication of pain can be defined as 'action', 'interaction' and 'transaction' (1). Whereas the 'action' can be considered to be the individual propensity or drive to display pain by overt behaviour, the 'interaction' and the 'transaction' both require the consideration of a receiver, who either only decodes the behavioural pain message or thereafter reacts to the sender, respectively. If 'interaction' or 'transaction' are the behavioural goals, the behavioural display of pain is likely subject to the relationship between the sender and receiver. Although facial responses represent one of the most prominent and informative nonverbal communication systems of pain, little is known about these relational effects. Previous findings indicate that children facially display pain to different degrees depending on the social partner in 'interaction' or 'transaction'. Thus, they show a higher degree of facial expressiveness in the presence of their parents, whereas they suppress their communication of pain in the presence of a stranger (2-4). The few studies involving adults reveal similar results, with participants suppressing their facial responses during pain when an unfamiliar observer is present (5,6). However, systematic investigations involving adults regarding the effects of no observer, 'strange' or 'familiar' observers on facial expressiveness remain lacking. In this context, certain characteristics of the partners in 'interaction' or 'transaction' may constitute critical influences. A variable that may be of influence and should be considered is the sex of the observer. This assumption is based on previous findings showing that another form of pain communication, namely subjective verbal pain report, can vary according to the sex of the recipient (7-9), with men reporting less pain if the observer is female.

As suggested earlier, pain communication can be seen as 'action', which refers to the individual propensity or drive to display pain. Such individual factors are likely to preform or modulate, in turn, the 'interaction' and 'transaction'. To date, empirical investigations on the effects of these individual factors have been scarce and have produced sometimes inconsistent results. Pain catastrophizing is – although not undisputedly – assumed to be associated with high pain expressiveness (1) and may, therefore, affect communicative 'action' and, in turn, both 'interaction' and 'transaction'. In accord, only children scoring low on pain catastrophizing appear to adapt the degree of facial expressiveness to the social setting, while high pain-catastrophizing children's expressiveness remains constant across situations (2,3). Another individual factor that likely influences the 'action' of pain

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communication and, thus, the 'interaction' and the 'transaction', is the sex of the individual displaying pain. This assumption can be derived from research investigating the facial display of other affective states, in which a modulating role of sex has been shown. Women (compared with men) facially display happiness and smiling to a higher degree (10,11), whereas they suppress the facial expression of anger and aggression (12-15). Interestingly, this enhancement and suppression, respectively, also depends on the social setting (and thus on 'interaction' and 'transaction') (10-15). Considering these results, it is conceivable that the degree of facial expressiveness during pain is also different in high and low pain catastrophizers, and in men and women. More importantly, these individual factors of the sender may again be differentially affected by social relationships.

When reviewing previous research investigating the impact of social relationships on facial responses to pain, it is clear that all studies have concentrated on the degree of facial expressiveness, which solely refers to the vigor and number of facial responses shown (16). However, facial responses to pain are not only characterized by the degree of expressiveness but also by the elements of the facial language used to communicate pain (types of facial responses). It is known that pain is signalled by a limited number of facial actions, which occur across different modalities of experimental pain (eg, cold, electrical current), as well as across experimental and clinical pain conditions in a seemingly uniform fashion (17,18). Due to this presumed consistency, the types of facial responses would not be expected to vary significantly depending on the recipient. However, even small variations within the limited number of facial actions may acheive communicative relevance. In the presence of an intimate other, an individual may, for example, favour signalling pain unpleasantness by eyebrow and levator contraction, whereas when alone, the same individual may selectively express the sensory dimension of his/her pain by contracting the muscles around the eyes (19). Thus, it appears reasonable to also determine whether the types of facial responses vary according to social relationships.

The aim of the present study was to further investigate how pain communication, considered as 'action', 'interaction' and 'transaction', is subject to changes in the relationship between sender and receiver. More precisely, we aimed to assess whether the types of facial responses occurring during painful stimulation and the degree of facial expressiveness vary among the following communicative relations: being alone (no observer, but aware of video recording); being with an experimenter (unfamiliar observer); and being with a partner (familiar observer). We hypothesized that the types of facial responses to pain would remain unaltered across the different situations (no qualitative changes of the facial pain language). On the other hand, we expected the degree of facial expressiveness during pain to be adapted to the relationship between participant and observer (only quantitative changes of the facial pain language). Given previous findings discussed above, we expected facial expressiveness to be reduced in the presence of the experimenter and to be elevated in the presence of an intimate other (in our case the partner). Furthermore, we considered pain catastrophizing and sex (of the participant and of the experimenter) to be additional critical influences on the effect that the relationship between sender and receiver has on the facial communication of pain.

METHODS

Participants

A total of 126 individuals (63 heterosexual couples; mean [± SD] age 39.9±13.5 years) participated in the current study. The participants were recruited via advertisements in the local newspaper (Bamberg, Germany). The advertisement recruited couples who had been in a relationship for >6 months (20,21). Exclusion criteria were current experience of acute or chronic pain, psychological or physical illnesses, and paresthesia or other types of somatosensory dysfunctions affecting the left lower leg (site of stimulation). Participants taking psychotropic drugs or analgesics were also excluded from participation. All participants provided informed consent and received monetary compensation. The study protocol was approved by the ethics committee of the University of Bamberg (Bamberg, Germany).

Procedure

The experiment consisted of three sessions using thermal stimulation of painful and nonpainful intensities. In one session, participants received thermal stimulation while they were alone in the room. During the other two sessions, another individual was present during the testing. This person was their partner in one session and an experimenter (male or female; randomly assigned) in another session. Thus, each subject was a participant in one session and an observer in another. Participants were informed that the focus of interest was how pain responses change across time and across social situations. Before testing started, the experimenter gave instructions, explained the following procedure and ensured everything was understood. The participants were asked to complete the German version of the Pain Catastrophizing Scale (PCS) at the end of the experiment, to avoid directing the participants' focus on pain-related thoughts before the painful stimulation.

Social manipulation

In the 'alone' session, the experimenter left the room immediately before thermal stimulation started. Participants were informed that the experimenter would be in the adjoining room and would return at the end of the stimulation session, or if they vocally signalled the need for anything. The participants were aware of being videorecorded (the video recording was kept constant across all three situations and, thus, participants were aware of video recording during all three sessions).

In the session with an experimenter present, the experimenter remained in the room and was seated in front of the computer controlling the thermal stimulation, which was located slightly on the right of the participant, approximately 2 m away. Participant and experimenter were facing one another and were able to have eye contact. However, the experimenter was instructed to avoid any verbal communication.

In the session with the partner present, the participant was in the room with his or her partner, seated slightly to the left, approximately 2 m away (without the experimenter being present). Similar to the session with an experimenter present, the participant and partner were facing one another and able to have eye contact, but were instructed not to talk to one another during stimulation. The seating positions of partner and experimenter resulted from the experimental setting, in which the experimenter sat in front of the computer controlling the thermal stimulation whereas the partner was seated away from the stimulator.

The order of the sessions was randomized across participants. The experiment always began with one partner undergoing all three sessions of thermal stimulation and then continued with the other partner as the participant. To avoid order effects, the female participant was tested first in 50% of the couples; in the other 50%, male participants were tested first.

Stimulation

Thermal stimulation was applied to three designated sites on the outer part of the left lower leg by a Peltier-based contact stimulation device (TSA-2001, Medoc, Israel) with a 30 mm × 30 mm contact thermode. The lower leg was chosen as the site for stimulation because it provides sufficient space to alter thermode placement between sessions and provided a rest period of at least 15 s between single stimuli; these two measures should prevent sensitization.

To ensure that temperature intensities were perceived as painful but not too painful in all participants (to prevent floor as well as ceiling effects), temperature intensities were tailored to the individual pain threshold. Thus, heat pain thresholds were determined first, using the method of adjustment. Participants were asked to adjust a temperature starting from 38°C, using heating and cooling buttons, until they obtained a level which was barely painful. A constant press of the buttons produced a heating or cooling rate of 0.5°C/s. Following a

familiarization trial, there were four trials and the average of these trials was used to constitute the threshold estimate.

Following the assessment of pain thresholds, phasic heat stimuli (5 s [plateau]; rate of change: 4°C/s; baseline temperature: 38°C; interstimulus intervals of 15 s to 20 s) were applied to the lower leg. Two different stimulus intensities were applied; namely, painful (+3°C above the pain threshold) and nonpainful (−3°C below the pain threshold) intensities. Applying nonpainful intensities allowed for the determination of which types of facial responses are specific for painful experiences. In each experimental session, participants received 10 painful and 10 nonpainful stimuli in random order.

Dependent variables

Self-report ratings: Participants were asked to provide self-report ratings using an electronic visual analogue scale (VAS; 100 mm), which appeared horizontally on a computer screen after each phasic stimulus. The scale was labelled with a verbal anchor of 'faintly painful' in the centre; thus, all nonpainful sensations should be rated below and all painful ones above. Participants were informed that the left and right ends of the scale corresponded to 'no sensation' and 'extremely strong pain', respectively. Participants were asked to rate the intensity of their nonpainful and painful experiences by moving the mouse cursor to the right or left, thereby choosing one location on the scale. This cursor appeared in a random location on the scale each time it was presented to avoid biases due to one-sided starting positions. Ratings had to be given within 10 s after stimulus offset.

Facial expression: Participant's faces were videotaped throughout the pain induction procedures. The camera was located approximately 1.0 m from the participant on top of the computer screen and participants were informed of the video recording. To enable offline segmentation of the videos, an LED light visible to the camera, but not to the participant, was lit concurrently with the 5 s thermal stimulation, beginning when the target temperature was reached. To ensure that the face would always be upright and in a frontal view during stimulation, participants were asked to look at the computer screen in front of them throughout the whole session and rate stimuli after they had appeared. Participants were also instructed not to talk during thermal stimulation

Facial expressions were coded from the video recordings using the Facial Action Coding System (FACS) (22), which is based on anatomical analysis of facial movements and distinguishes 44 different 'action units' (AUs) produced by single muscles or combinations of muscles. Three coders, trained by a certified FACS coder (qualified by passing an examination given by the developers of the system) identified the frequency and the intensity (five-point scale) of the different AUs (inter-rater reliability, calculated using the Ekman-Friesen formula [22], was between 0.84 and 0.87). Software designed for the analysis of observational data (Observer Video-Pro; Noldus Information Technology, Netherlands) was used to segment the videos and to enter the FACS codes into a time-related database. Time segments of 5 s beginning just after the stimulus had reached the target temperature (time period during which the LED was lit) were selected for scoring. In total, 3 × 20 segments of thermal stimulation (10 nonpainful and 10 painful segments in three sessions) were analyzed for each participant. For the purpose of necessary data reduction, AUs that represent facial movements of the same muscle were combined, as has been performed in previous studies without any loss of information (23,24). Those combinations include AU 1/2, 6/7, 9/10 and 25/26/27.

Independent variables

Pain catastrophizing: A German translation of the PCS was used to assess catastrophic thinking related to pain (25). Participants were instructed to reflect on thoughts or feelings during the past painful experiences. The scale contains 13 items that are rated on a five-point scale, with the end points 'not at all' and 'all the time'. The PCS has been widely used in research on pain catastrophizing, and has been shown to have high internal consistency (Cronbach's α=0.87) (25,26).

Sex: In addition to the PCS score, sex of the experimenter and participant were considered and used as independent variables in the following analyses.

Statistical analyses

Because participants were recruited as couples, the population investigated in the current study cannot be considered to be a perfect random sample. Thus, as well as being a participant who experienced pain, each participant was also once the observer. To exclude that the degree of facial expressiveness of those participants who first served as an observer was influenced by observing their partners' degree of facial expressiveness, the association between the partners' degree of facial expressiveness was assessed. This was performed by correlating the degree of facial expressiveness (composite score; see 'Degree of facial expressiveness' below) between partners separately for all three situations. None of these correlations were significant (all $P>0.05$). In addition, when correlating the single AUs (AU 4, 6/7, 9/10) separately, which were later aggregated into the composite score, none of the correlations between partners were significant (all $P>0.05$). This was the case for all three situations. Therefore, a lack of independence of the data cannot be assumed, which, in the following analyses, allows the participants to be treated as individuals who had been recruited by conventional sample methods.

Effect of communicative relations on pain responses

Self-report: The impact of communicative relations (alone, in the presence of the experimenter or in the presence of the partner) on subjective pain ratings was investigated using repeated-measures ANOVA (dependent variable: VAS ratings; within-subject factor: communicative relation).

Facial expression: *Types of facial responses:* One aim of the present study was to assess whether different types of facial responses occur during painful stimulation depending on the communicative relation. This was assessed by first determining which AUs were displayed in each of the three social situations at a frequency >5% (of the painful segments). The critical margin of 5% was derived from earlier studies (23,27-31). Subsequently, whether the frequency distribution of these AUs was comparable in all three social situations (alone, with partner and with experimenter) was analyzed. To test for differences in frequency distribution of AUs (percentage of occurrence of each AU) among social situations, χ^2 analyses were conducted comparing distributions between alone versus experimenter, alone versus partner and experimenter versus partner.

Moreover, which of the AUs with an occurrence frequency >5% were truly pain indicative and whether different AUs may be pain indicative in different communicative relations was determined. To determine this, effect sizes (Cohen's d for repeated measures) contrasting occurrence frequencies of each AU between painful and nonpainful trials were computed. This was calculated separately for each social situation. AUs showing an effect size of $d\geq0.5$ (medium effect) were selected as pain-indicative facial responses, and whether the same AUs proved to be pain indicative in all three social situations was descriptively compared.

Degree of facial expressiveness: In addition to comparing the types of facial responses to pain between social situations, whether the degree of facial expressiveness was affected by the type of relationship between the participant and observer was also investigated. To do this, all AUs that proved to be pain-indicative (see description above) across all three social situations were combined into one composite score of pain-relevant facial responses. The composite score was calculated by first combining the frequency and intensity values of each AU to product terms (19,23). Second, the product terms of all pain-relevant AUs were averaged. Finally, the averaged product terms were square-root transformed to yield unskewed composite scores of pain-relevant facial responses, as has been performed in previous studies (19,24). Composite scores were calculated for each of the three situations separately. Therefore, it was possible to conduct a repeated-measures ANOVA to assess the effect of communicative relations (alone, with partner and with experimenter) on the composite scores of pain-relevant AUs (degree of facial expressiveness).

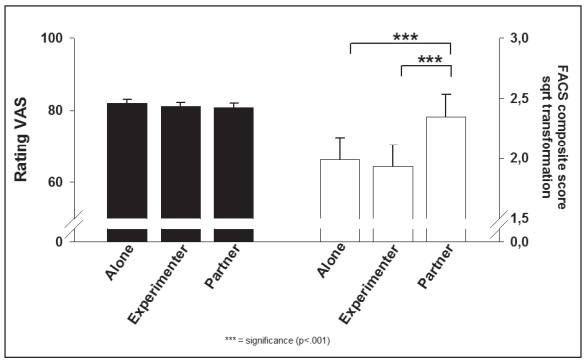

Figure 1) *Mean ± SEM values for visual analogue scale (VAS) ratings of subjective pain intensity (left); and composite scores (square-root [sqrt] transformed) of evoked (pain-relevant) facial expressiveness in response to painful heat stimulation (right). Values are given separately for all three social situations (alone, experimenter and partner). FACS Facial Action Coding System*

TABLE 1
Facial Action Units (AUs) with a critical frequency of occurrence >5% in painful segments. Data are presented for each social situation

	Alone		Partner		Experimenter	
AU	Percent*	Effect size	Percent*	Effect size	Percent*	Effect size
AU 1/2	14.1	0.2	18.6	0.3	12.0	0.3
AU 4	29.2	**0.7**	35.2	**0.9**	29.8	**0.7**
AU6/7	44.5	**0.6**	55.2	**0.7**	44.0	**0.7**
AU 9/10	24.0	**0.5**	25.3	**0.5**	19.8	**0.6**
AU 12	7.8	0.4	13.0	0.2	–	–
AU 14	11.4	0.1	10.5	0.0	14.1	0.3
AU 17	5.0	0.1	8.1	0.2	6.9	0.2
AU 18	8.2	**0.5**	7.1	**0.5**	6.1	0.3
AU 23	5.8	0.2	5.6	0.3	6.0	0.3
AU 25/26	35.3	**0.6**	29.6	0.4	27.2	0.3

*Effect sizes for frequency differences between nonpainful and painful segments are given. Medium and strong effect sizes (d≥0.5) are marked in bold. *Denotes the percentage of occurrence in the entire painful segments*

Additional influences

To determine whether the effect of communicative relations on the degree of facial expressiveness was also affected by other factors (ie, pain catastrophizing, sex of the participant and sex of the experimenter), additional analyses were necessary. To determine how those factors affected the changes in the degree of facial expressiveness, change scores of facial expressiveness between social situations were calculated to serve as dependent variables. This approach was also necessary due to the study design. Because the sex of the experimenter was only present as a variable in the experimenter session and, thus, could not have affected facial expressiveness when participants were alone or with their partner, including all three factors in one comprehensive analysis was not possible. Therefore, change scores of facial expressiveness between the social situations were calculated with the 'alone' condition serving as baseline and fed into two distinct analyses, investigating:

- the change in expressiveness from being alone to being with the experimenter: An ANOVA was performed to determine whether the change in expressiveness from being alone to being with the experimenter (difference score: experimenter – alone) was influenced by the sex of the participant and by the sex of the experimenter, as well as by pain catastrophizing (median split of PCS score). All three variables were entered as independent variables into the ANOVA; and
- the change in expressiveness from being alone to being with their partner: This second ANOVA examined whether variations in expressiveness from being alone to being with their partner (difference score: partner – alone) were influenced by the sex of the participant (as previously mentioned, the sex of the observer was of no interest in this context because only heterosexual couples were evaluated and, thus, the sex of the observer was always opposite to the sex of the participant) and by pain catastrophizing (median split of PCS score). Both variables were entered as independent variables into the ANOVA.

Because these ANOVAs used change scores, whether PCS, sex of the participant and sex of the experimenter affected the degree of facial expressiveness in general could not be determined. Therefore, *t* tests assessing the general influence of sex and PCS on overall facial expressiveness (composite score merged over all three situations) were also computed.

Results for the within-factor analyses were corrected according to Greenhouse-Geisser whenever the Mauchly test of sphericity indicated heterogeneity of covariance. For ANOVAs showing significance, post hoc *t* tests were calculated. Findings were considered to be statistically significant at $\alpha<0.05$. In addition to P values, partial eta-squared (η_p^2) and Cohen's d as measures of effect size were also reported.

RESULTS

In the present study, 63 heterosexual couples (n=126) were tested. The mean age of the participants was 39.9±13.5 years and the mean length of the relationship was 14.8±13.3 years; mean pain threshold was 46.3±1.2°C. Given the healthy and pain-free sample of individuals tested, it is not surprising that the median score of the PCS was fairly low (14.0). Accordingly, the subjects were separated into two groups based on the median split: 'low' (PCS score range 0 to 14) and 'moderate' (PCS score range 15 to 36) pain catastrophizers. The two groups did not differ significantly with regard to age and pain threshold (all P>0.6). In addition, there were almost equal numbers of male and female participants in each group (low PCS group, 49.3% female participants; moderate PCS group, 52.5% female participants).

Effect of communicative relations on pain responses

Self-report: Self-report ratings, as provided by the VAS, did not change across social situations (F[2, 250]=1.528, P=0.219, η=0.012) (Figure 1). On average, participants rated painful stimulation as 82.0±11.7 when being alone, 81.1±13.1 when in the presence of the experimenter and 80.8±12.8 when with their partner (on a scale ranging from 0 to 100, with 50 representing 'faintly painful').

Facial expression: *Types of facial responses to pain:* There were only very minor frequency differences among the three social situations with regard to the types of facial responses to pain occurring with a frequency of >5% (Table 1). With the exception of AU 12 (which did not occur above the critical level of >5% in the experimenter situation), the same AUs were displayed independently of the communicative relation. Moreover, when comparing the frequency distribution of those AUs between situations (χ^2 analyses of frequencies), no differences were observed. The distribution of AUs when being alone did not significantly differ from the AU distribution in the presence of the partner (χ^2=1.59; P=0.991) or in the presence of an experimenter (χ^2=1.207; P=0.997). The distribution of AUs did also not significantly differ between the 'partner' and 'experimenter' session (χ^2=1.262; P=0.996). Brow lowering (AU 4), orbit tightening (AU 6/7) and levator contraction (AU 9/10) were the facial responses displayed most frequently regardless of the social situation. Moreover, when considering which of the AUs proved to be indicative of pain in each of the three situations (effect sizes ≥0.5 for the difference in frequency between nonpainful and painful stimulation), high agreement was again observed among the social situations (Table 1). Therefore, the type of relationship between the participant (sender) and observer does not appear to have a strong effect on the types of facial responses being elicited during pain.

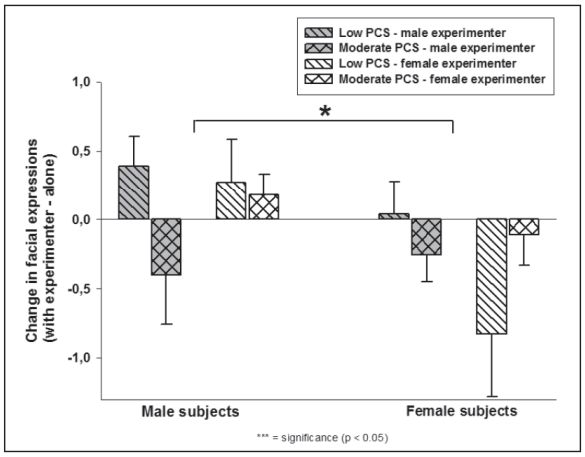

Figure 2) *Change scores of facial expressiveness (difference of the composite scores of facial expressiveness (square-root transformed) in the situations 'experimenter – alone'; mean ± SEM values. Scores are presented separately for male and female participants as well as experimenters, and for low and moderate pain catastrophizers. PCS Pain Catastrophizing Scale*

Degree of facial expressiveness: When investigating whether the communicative relation affects the degree of facial expressiveness, however, major differences were apparent. The composite score consisting of the AUs that were indicative of pain in all three situations (brow lowering [AU 4], orbit tightening [AU 6/7] and levator contraction [AU9/10]) differed substantially among the situations ($F[2, 250]=9.771$, $P<0.001$, $\eta=0.072$) (Figure 1). Post hoc testing showed that, in the presence of the partner, participants significantly increased the degree of facial expressiveness (elevated composite score) compared with being alone ($t[126]=-3.64$, $P<0.001$) or in the presence of the experimenter ($t[126]=-3.82$, $P<0.001$). When comparing the situation of being alone with the presence of the experimenter, no significant differences were observed ($t[126]=0.56$, $P=0.574$).

Additional influences

Alone versus experimenter: Results of the additional ANOVA analyzing the influence of participant sex and experimenter sex, as well as the participant's PCS level on the change of facial expressiveness due to the presence of an experimenter compared with being alone, are presented in Figure 2.

The only main effect that reached significance was the sex of the participant ($F[1, 124]=4.025$, $P=0.047$, $\eta=0.034$). As shown in Figure 2, the change score of female participants was almost consistently negative, while that of male participants varied but tended to be positive. Thus, female participants reduced their facial expressiveness during painful stimulation in the presence of an experimenter compared with being alone, while male participants showed no consistent change in expressiveness (Figure 3). By itself, neither the sex of the experimenter ($F[1, 124]=0.112$, $P=0.739$) nor the PCS score ($F[1, 124]=0.345$, $P=0.558$) had a significant influence. The two-way interaction between those factors, however, reached significance ($F[1, 124]=4.635$, $P=0.033$, $\eta=0.038$). Pairwise comparisons showed that this effect was solely caused by the significant differences between moderate and low pain catastrophizers in the presence of a male experimenter ($t[65]=-2.056$, $P=0.044$). Compared with low pain catastrophizers, moderate pain catastrophizers decreased their facial expressiveness when a male experimenter was present. Aside from this interaction, none were significant (all $P>0.05$).

Alone versus partner: Results of the additional ANOVA concerning the influence of the sex of the participant and the participant's PCS level on the change of facial expressiveness due to the presence of the partner compared with being alone are presented in Figure 4. Given that the experimenter was neither present in the 'alone' nor in the 'partner' situation, the sex of the experimenter was not considered in this analysis.

Neither the PCS score ($F[1, 124]=0.158$; $P=0.692$) nor the sex of the participant ($F[1, 124]=0.712$; $P=0.401$) had an impact on the change in facial expressiveness in the presence of a partner compared with being alone. Furthermore, there was no significant interaction between these factors (all $P>0.05$).

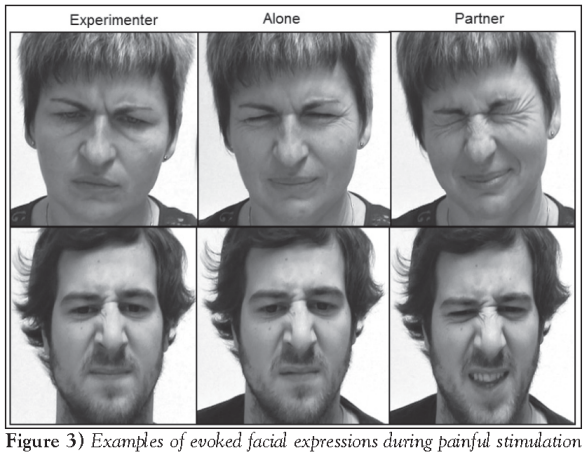

Figure 3) *Examples of evoked facial expressions during painful stimulation in each of the three social situations by a female (upper row) and male participant (lower row)*

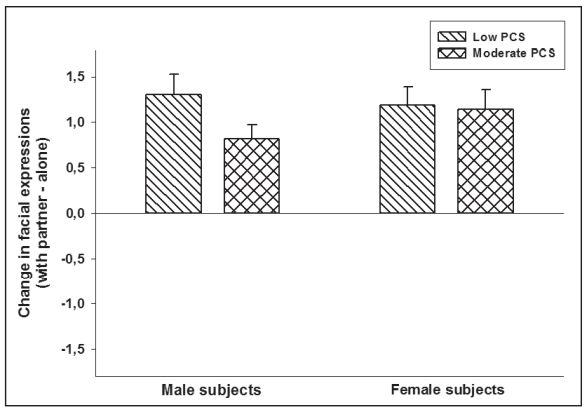

Figure 4) *Change scores of facial expressiveness (difference of the composite scores of facial expressiveness (square-root transformed) in the situations 'partner – alone'; Mean values (± SEM). Scores are presented separately for male and female participants and for low and moderate pain catastrophizers*

General effects of individual participant factors (sex and PCS)

The general effects of participant sex and pain catastrophizing on the overall degree of facial expressiveness were also evaluated independent of the social situations. *t* tests for independent samples showed that neither PCS nor sex of the participant had a significant general impact on facial expressiveness during painful stimulation (all $P>0.15$).

DISCUSSION

The present study was designed to investigate whether, and how, different communicative relations (alone [but aware of video recording], with the partner, with an experimenter) affect facial responses to pain

in healthy adults. Our results indicate that pain is signalled by the same types of facial responses independent of the type of relationship between participant (sender) and observer. However, the degree of facial expressiveness, which represents the strength of the social signal, varied and was apparently adjusted according to social rules. In other words, facial responses to pain appeared to be similar when participants were alone, with a stranger or with an intimate partner; however, the intensity of the response varied dependently on the recipient. These findings will be discussed in detail below.

Effect of communicative relations

The effect of communicative relations on facial responses to pain was investigated by considering the types of facial responses and the degree of facial expressiveness.

With regard to the types of facial responses, we found no significant differences among the three situations. As expected, similar types of facial responses to pain were elicited with similar percentage distributions regardless of the type of relationship between participant (sender) and observer. These responses included the lowering of the brow (AU 4), orbit tightening (AU 6/7) and levator contraction (AU 9/10), all of which have been previously reported in the context of pain (16,17,32). Given that the facial response to pain has to be recognized with high certainty – to fulfill its 'interactional' and 'transactional' goals (1,33) – finding it to be unchanged across social situations seems reasonable. If the communicative relation fundamentally changes the types of facial responses being elicited during pain, the certainty of recognition in 'interaction' and 'transaction' may be endangered. Therefore, displaying the same types of responses independently of the relationship between sender and observer most likely preserves the essential recognisability of the facial expression of pain.

However, we found the degree of facial expressivenessto be significantly affected by communicative relations. Whereas the degree of facial expressiveness was significantly elevated when an intimate other, in this case the partner, was present, the presence of the experimenter caused a tendency to reduce facial expressiveness (only in women). Accordingly, individuals appear to adjust the vigor and number of their facial responses depending on the relationship between sender and observer and, thus, depending on the different 'interactional' and 'transactional' goals.

A similar effect has been shown for other affective states (eg, anger, joy) and has been interpreted in terms of so-called 'social display rules'. These display rules define whether and how an expression of emotion is culturally appropriate in a given social situation (13,15,34,35). For example, in the presence of a formal other (eg, teacher, experimenter) it seems less appropriate to overtly show one's emotions (35,36), whereas emotions can be communicated more openly toward intimate others (eg, parent or friend) (35,37). Our results, along with previous findings in children (2,3), indicate that the facial expression of pain follows similar situational standards. When being in the presence of an intimate other – the partner (our study) or a parent (2,3) – individuals appear to communicate their pain more strongly via facial expressions compared with being alone or in the presence of a stranger. Why might it be an advantage to adapt one's facial expressiveness during pain dependent on the recipient?

Given that facial responses to pain can be a powerful means of eliciting empathy and social support in the observer (33,38), it is reasonable to communicate pain to a higher extent toward observers who are sympathetic, because they are the ones who would most likely provide help. Consistent with this, it has been shown that the amount of time that two individuals commonly spend with one another predicts whether these individuals attend to and correctly interpret one another's pain behaviour (39). Therefore, it seems sensible for an individual to display pain more openly toward those observers whom they spend a lot of time with – such as the partner – and who may be more willing to attend to and more able to decode the sent message. On the other hand, it has been hypothesized that showing vulnerability by signalling pain to observers whose reactions one cannot predict (an unfamiliar other) may endanger the individual who is experiencing pain (33,40,41).

When interpreting the current data, it has to be noted that participants were aware of video recording during all aspects of the experiment and, thus, participants may have felt 'observed' in all three conditions. However, this awareness of being observed by a camera may have interfered in particular with the experimental goal in the 'alone' situation, in which we aimed to assess the individual when he/she believed they were alone or, in other words, unobserved. Therefore, the degree of facial expressiveness in our 'alone' situation may have been lower than when participants were truly convinced they were alone and completely unobserved. This, in turn, may have contributed to the lack of differences when comparing the expressiveness in the presence of an unfamiliar other (the 'experimenter' situation) with the 'alone' situation.

Additional influences on the effect of communicative relations

Alone versus experimenter: The change in the degree of expressiveness due to the presence of the experimenter was significantly influenced by the sex of the participant. Women – in contrast to men – significantly decreased the degree of facial expressiveness during pain in the presence of an experimenter compared with being alone. This finding is consistent with previous findings on sex differences in social display rules. In front of an unfamiliar other, females facially express positive affective states, such as happiness, to a higher degree, whereas they conceal negative ones such as anger (11-13,15,35). Given that pain is a rather negative affective state, the decrease of womens' facial expressiveness in the presence of an experimenter is consistent with these previous results.

As opposed to the sex of the participant, there was no main effect found for the sex of the experimenter. Participants showed comparable levels of facial expressiveness, regardless of whether the experimenter was male or female. This result is inconsistent with previous findings on subjective pain reports, which have shown that male research participants rate stimuli as less painful when being tested by a female compared with a male experimenter (7-9). It is possible that facial and subjective pain responses are differentially affected by the sex of the experimenter. Moreover, previous studies more strongly emphasized gender roles (by specific clothing and behaviour) than we did (42) and, thus, we may have neutralized gender roles.

Earlier studies found pain catastrophizing to moderate the effect that familiar or unfamiliar observers may have on facial expressiveness (2,3,6). However, similar to a previous study of ours (23), pain catastrophizing neither had an effect on the overall degree of facial expressiveness nor on the effect of familiarity of observer (communicative relations) on this parameter in the present study. The reason for this inconsistency may originate in methodical differences such as the type of participants (children versus adults), type of pain stimulation (fixed physical versus psychophysically adjusted stimulus intensities) and type of facial analysis (Children Facial Coding System (43) versus FACS). We found a significant interaction only between catastrophizing and sex of the experimenter. Rather puzzlingly, moderate pain catastrophizers, compared with low catastrophizers, reduced the degree of facial expressiveness in the presence of a male experimenter. Therefore, further research seems necessary to specify whether and how pain catastrophizing plays a role in modulating the effects of communicative relations on facial responses to pain.

Alone versus partner: The shift to stronger facial expressiveness in the presence of a partner was neither influenced by pain catastrophizing nor by the sex of the participant. We speculate that the drive to signal pain to the partner is so pronounced that variables, such as sex and pain catastrophizing, cannot add to that and, thus, become less relevant.

Self report

In addition, we assessed self-report ratings to control whether differences in facial responses between situations are simply caused by

differences in subjective experiences. To minimize the impact of communicative relations on self-report ratings, a computerized assessment was performed, with research participants always rating the stimuli on a computer screen that was neither visible to the partner nor to the experimenter. Given that self-report ratings did not change between social situations, we can exclude the possibility that the observed changes in facial expressiveness are only due to changes in subjective pain experience.

Limitations

As mentioned above, one limitation to the present study is the fact that participants also knew that they were being filmed when being alone. In future replications, it would be interesting to also include a condition in which participants genuinely believe themselves to be alone; however, due to ethics constraints, this would be difficult to perform.

Another limitation to the current study was the arrangement of seating positions in the experimental room. The experimenter always sat contralateral whereas the partner always sat ipsilateral to the stimulation site. As has been shown (44), the resulting different eye orientations during stimulation may have affected our results. However, finding no differences in self-report ratings between the situations appears to contradict this assumption.

In addition, the special feature of having tested couples has been underused in the current study because, for the purposes of the present study, this form of recruitment only guaranteed the familiarity of the partner but was not considered for other aspects of partnership. We may be able to deliver these data at a later point.

As a final point of potential criticism, we grouped our subjects into 'low' and 'moderate' PCS scorers by using the median as cut-off, which is a somewhat arbitrary criterion. Furthermore, this approach, which we preferred for its good illustrative properties, reduced individual differences. However, even when using raw PCS scores in a regression design the same results evolve, with PCS scores neither being able to predict significantly the change of facial expressiveness between being 'alone' and 'with the experimenter' nor the change of facial expressiveness between being 'alone' and 'with the partner' (all $P>0.05$). Therefore, we can exclude the possibility of crucial information loss due to using the median-split approach.

CONCLUSION

Independently of the recipient, pain is signalled via the same types of facial responses. Thus, the elements of the facial language used to communicate pain remain unaltered by the relationship between sender and observer, which may guarantee reliable recognition. However, the degree of facial expressiveness changes depending on the communicative relations, with increasing expressiveness occurring in the presence of an intimate other. This appears to be beneficial because sympathetic observers may be able to more quickly identify painful experiences and, therefore, the possibility of receiving help is elevated. Interestingly, when confronted with an unfamiliar individual, the two sexes appear to pursue different 'interactional' or 'transactional' goals. Whereas men do not alter the degree of facial expressiveness when being observed by an experimenter (compared with being alone), women reduce their degree of facial expressiveness, possibly due to learned display rules that make the overt display of negative affect in women seem inappropriate.

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