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Motor Function Responses to Induced Pain and Cryotherapy

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MOTOR FUNCTION RESPONSES TO INDUCED PAIN AND CRYOTHERAPY

by

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A dissertation submitted to the faculty of

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in partial fulfillment of the requirements for the degree of

Doctor of Philosophy

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ABSTRACT

MOTOR FUNCTION RESPONSES TO INDUCED PAIN AND CRYOTHERAPY

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Objective: Establish and validate an experimental pain model that will create pain for at least 20-minutes and then use the model to determine if: 1) cryotherapy decreases experimentally induced pain, 2) experimentally induced pain contributes to arthrogenic muscle inhibition, and 3) cold application influences pain or arthrogenic muscle inhibition. To answer these questions we conducted two experiments, the results of which are presented in two manuscripts. *Methods:* Seventy (n = 30 for experiment I and n = 40 for experiment II), physically active healthy male subjects participated. *Interventions:* Independent variables used for experiment I were condition (5% hypertonic saline infusion/cryotherapy, no-saline infusion/cryotherapy, 5% hypertonic saline infusion/sham) and time (precondition, every minute during a condition, and 10 minutes following each condition). For experiment II, independent variables were treatment (saline infusion, saline infusion/cryotherapy, saline infusion/sham, and no-saline infusion) and time (pretreatment, posttreatment, and 30-minutes posttreatment). Dependent variables measured were pain perception, knee surface and ambient

temperatures, and H_{max}, and M_{max} measures (experiment II only). *Results:* Saline caused more pain than no-saline at minutes 3, 4, and 5 during infusion. Pain caused by saline and sham application remained constant from 4 minutes during application through 1 minute following application. Cold application decreased pain for 16 minutes. Pain resulted in arthrogenic muscle inhibition following and 30 minutes following saline infusion. Cryotherapy removed inhibition following but not 30 minutes following application. Pain for the saline groups increased following infusion as measured with the pain rating index and visual analogue scale. According to pain rating index, cryotherapy did not decrease pain; however, cryotherapy decreased pain as measured with the visual analogue scales. No change in temperature occurred during the non-cooling conditions. Ambient temperatures fluctuated less than 1°C. *Conclusion:* Saline infusion caused anterior knee pain for over 20 minutes and resulted in arthrogenic muscle inhibition. Cryotherapy disinhibited the quadriceps motoneuron pool and reduced pain as measured with visual analogue scales. Cryotherapy did not decrease pain as measured with the McGill pain questionnaire.

BRIGHAM YOUNG UNIVERSITY

GRADUATE COMMITTEE APPROVAL

of a dissertation submitted by

Blaine C. Long

This dissertation has been read by each member of the following graduate committee and by a majority vote has been found to be satisfactory.

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As chair of the candidate's graduate committee, I have read the dissertation of Blaine C. Long in its final form and found that (1) its format, citations, and bibliographical style are consistent and acceptable and fulfill university and department style requirements; (2) its illustrative materials including figures, tables, and charts are in place; and (3) the final manuscript is satisfactory to the graduate committee and is ready for submission to the university library.

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Kenneth L. Knight
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Intermittent infusion of 5% hypertonic saline produces consistent pain while cryotherapy decreases the pain

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There are 23 text pages for the entire manuscript including 2 Tables and 4 Figures.

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Abstract

Objective: Establish an experimental pain model that lasts 20 minutes and determine if cryotherapy decreases the pain. *Methods:* Thirty, physically active healthy male subjects participated in this 3x36 randomized controlled laboratory study. *Interventions:* The following independent variables; condition (5% hypertonic saline infusion/cryotherapy, no-saline infusion/cryotherapy, 5% hypertonic saline infusion/sham) and time (precondition, every minute during a condition, and 10 minutes following each condition) were used to determine if they influence pain perception (VAS) and temperature. *Results:* There was a significant interaction between condition and time ($F_{68,864}$=3.0; *P*=.0001). During the 5 minute preapplication, the saline infusion/cryotherapy and saline infusion/sham conditions experienced more pain than no-saline infusion condition at minutes 3, 4, and 5. Pain for the saline/sham condition remained constant from 4 minutes during application through 1 minute following application. As compared to the saline infusion/sham condition, cold application decreased pain for 16 minutes in the saline infusion/cryotherapy condition. There was no difference in preapplication surface temperature for each condition. No change in temperature occurred during the saline infusion/sham condition. Cooling and rewarming were similar in the cryotherapy conditions. Ambient temperature fluctuated less than 1°C during data collection. *Conclusion:* Saline infusion caused pain for over 20 minutes. Cryotherapy decreased the pain for 16 minutes. This model may be useful in examining pain on skeletal muscle activation and the effectiveness of various interventions on pain.

Keywords: 5% hypertonic saline, Intermittent Infusion, Pain, Cryotherapy

1. Introduction

Experimental pain models often involve a single injection (Graven-Nielsen et al., 2000; Bennell et al., 2004) or constant infusion of sterile 5% hypertonic saline (Graven-Nielsen et al., 1997; Thunberg et al., 2005). Single injections in the infrapatellar fat pad produce a gradual onset and rapid decline of pain in about 15 minutes (Bennell et al., 2004). Constant infusion has been delivered into skeletal muscle with various infusion rates and volumes (Graven-Nielsen et al., 1997; Svensson et al., 1998; Matre et al., 2002; Farina et al., 2005; Thunberg et al., 2005). Some include short infusions lasting about 20 to 40 seconds (Svensson et al., 1998; Le Pera et al., 2001; Farina et al., 2004) while others involve infusions lasting 20 minutes (Thunberg et al., 2005).

Since single injections of 5% hypertonic saline do not create pain for at least 20 minutes, they would be inadequate when examining the effectiveness of a cryotherapy treatment. Cryotherapy is often applied for at least 20 minutes to minimize pain during rehabilitation (Airaksinen et al., 2003; Bleakley et al., 2004; Saito et al., 2004; Koç et al., 2006). Investigating cryotherapy and its influence on pain has been difficult due to injury differences and patient subjectivity. Injured patients often have pain intensities that fluctuate in severity thus making pain difficult to quantify. Therefore, an experimental pain model that causes at least 20-minutes of anterior knee pain is needed to determine the effectiveness of a cryotherapy treatment on pain.

Constant infusion causes pain in skeletal muscle for at least 20-minutes (Thunberg et al., 2005). When examining this method on pain arising from the

infrapatellar fat pad, it causes too much pain within the first 5 minutes of infusion, resulting in a subject's decision to discontinue their participation (unpublished results).

The purposes of this investigation, therefore, were too: 1) determine if an intermittent infusion of 5% hypertonic saline into the infrapatellar fat pad causes pain that lasts over 20 minutes and 2) determine if a 20-minute cryotherapy application during a intermittent infusion of 5% hypertonic saline into the infrapatellar fat pad decreases pain.

2. Methods

2.1 Study design

A 3 x 36 randomized controlled laboratory study with repeated measures on time guided data collection. Independent variables were condition [(saline infusion/ cryotherapy (saline/cryo), no-saline infusion/cryotherapy (no-saline/cryo), and saline infusion/sham (saline/sham)] and time (every minute during a preapplication (6), application (20) and for 10 minutes postapplication (10)). The dependent variable was perceived pain (visual analogue scale; VAS). Additionally, to determine if the same level of cooling in the cryotherapy conditions, and that temperature remained constant for the saline/sham condition, patella and popliteal surface temperatures were measured every minute during preapplication, application, and postapplication.

2.2 Subjects

Thirty, physically active, healthy, male subjects (age = 23.0 ± 3.25 yrs, ht = 180.92 ± 5.87 cm, mass = 81.3 ± 15.9 kg) volunteered to participate in this investigation. Each subject went through a short orientation session prior to their participation. The orientation consisted of an explanation of the experiment including the VAS and risks

and benefits of the study. Subjects then filled out a preparticipation health history questionnaire to ensure they were free from any lower extremity orthopedic, neurological, cardiovascular, or endocrine pathology. The study was approved by the institutional review board (IRB) and subjects gave written informed consent prior to being randomly assigned to 1 of the 3 conditions.

2.3 Instruments

Pain was induced with an implanted 24 gauge x 0.75 in (0.7 x 19 mm) Teflon catheter (Alliance Medical, Russellville, MO) or implanted catheter with simultaneous infusion of 5% hypertonic saline (B. Braun Medical, Inc., Irvine, CA). To infuse hypertonic saline, a 30 cm extension set (B. Braun, Medical Inc, Bethlehem, PA) was interfaced between the Teflon catheter and a 5 cc syringe filled with 5% hypertonic saline. The syringe was positioned in a constant infusion pump (Harvard Apparatus, Millis, MA; model # 975) used to intermittently deliver saline over 25 minutes. Infusion rate was 0.54 cc/minute during 5 consecutive on and off cycles. Each on/off cycle was 3 minutes with an exception of the last minute being "on." Total volume of saline infused consisted of 7.02 cc. Once the first 5 cc syringe was emptied, we exchanged the syringe with a second 5 cc syringe filled with hypertonic saline during an "off" cycle.

Pain perception was measured with a 100 mm VAS. The VAS was labeled "no pain" on the left polar end and "unbearable pain" on the right polar end (Mattacola et al., 1997). When measures are taken every minute, the VAS is reported to be reliable tool in assessing acute pain ($r = 0.87$) (Bijur et al., 2001).

Surface temperature was measured with three PT-6 Kapton insulated thermocouples (Physitemp Instruments, Inc., Clifton, NJ) interfaced to 3 channels in a 16-channel Iso-Thermex electrothermometer (Columbus Instruments, Columbus, OH). A plastic bottle with a hole on each end and in the center was positioned on a pillow in the popliteal fossa to minimize interface temperature between the popliteal fossa and the pillow (Figure 1) during baseline and postapplication measures. Data were stored in a desktop computer interfaced with the Iso-Thermex electrothermometer. Temperatures were recorded every minute throughout data collection in conjunction with pain data.

2.4 Testing procedures

Subjects reported to the laboratory dressed in shorts and a T-shirt. Upon arrival, they were positioned supine on a treatment table with their dominant leg (i.e. leg with which they kick a ball) slightly bent. A baseline pain perception measure was then reported with a vertical mark placed on the 100 mm VAS.

Two 2.5 X 2.5 cm areas; one over the patella and the other in the center of the popliteal fossa, were shaved and cleansed with isopropyl alcohol for surface thermocouple application. One thermocouple was secured to the center of the patella and the other in the center of the popliteal fossa.

A small area inferiolateral to the patella was shaved and cleansed with 70% isopropyl alcohol and povidone-iodine solution for catheter needle insertion. In order to find the infrapatellar fat pad, the lateral border of the patellar tendon was palpated. The catheter needle was then inserted deep to the patellar tendon to a depth of 19 mm. Once

inserted, the needle was extracted leaving the flexible Teflon catheter implanted in the infrapatellar fat pad (Figure 1).

For the saline/cryo and sham groups, saline was intermittently infused over 25 minutes. At minute 5 during intermittent infusion, the pillow and plastic bottle were removed from the posterior side of the knee joint and two 1-kg bags of crushed ice or cat litter (sham bags) were secured to the knee joint with a double 6-inch elastic wrap for 20 minutes (Figure 2). One bag was applied to the anterior surface of the knee joint and the other bag was applied to the posterior surface of the knee joint. The no-saline/cryo group also received ice bags at the same time intervals as the saline/cryo group.

Following the 20-minute application, the ice bags or sham bags were removed and subjects remained on the table for an additional 10 minutes. During the 10-minute postapplication period, subjects continued to report their perceived pain on new VASs every minute. A timeline for data collection is presented in Figure 3.

Immediately following the postapplication phase, the 30-cm connection tube was disconnected from the Teflon catheter, the catheter was extracted from the infrapatellar fat pad, and the catheter insertion site was treated with antibiotic ointment and a Band-Aid.

Following the wound treatment and 24 hours after the investigation, we contacted each subjects to see if they were experiencing any lingering pain from the infused hypertonic saline or inserted Teflon catheter.

2.5 Statistical Analysis

Descriptive statistics were computed for the 4 measurement variables: perceived pain (VASs), surface temperature at the patella and popliteal fossa, and ambient temperature. All surface temperature data are presented by application phase. Pain perception was analyzed and presented for each minute.

We used 3 X 36 (condition x time) mixed model ANOVAs with random effects for subjects and within-subject order-1 autoregressive (AR-1) (Vamoş et al., 2007) correlations, one for each measurement variable, to determine if there were differences between conditions across time. We also used AR-1 correlations to determine if the subsequent pain measures changed within each condition across time.

Tukey-Kramer post hoc multiple comparison tests were used to examine individual differences in perceived pain and surface temperature. For all differences, the level of significance was set at $P < .05$. Data were analyzed with the MIXED procedures of Statistical Analytical Software (SAS; 9.1 Carey, North Carolina).

Thermocouple uncertainty (validity + reliability) was computed for the 3 thermocouples according to Jutte et al.(Jutte et al., 2005; Jutte et al., 2008)

3. Results

3.1 Pain perception

There was a significant interaction between condition and time for perceived pain ($F_{68,864} = 3.0$; $P = .0001$). During the 5-minute preapplication, perceived pain at minutes 3, 4, and 5 in the two saline conditions were higher than the no-infusion condition (TK, $P < .001$).

At minute 5, the saline/cryo condition experienced more pain than saline/sham condition ($F_{1,864} = 6.0$; $P = .03$). Pain in the saline/sham condition remained constant from 4 minutes during application through 1 minute following application (17 minutes; Figure 4). As compared to the saline/sham condition, the saline/cryo condition had a significant decrease in perceived pain from 11 minutes during application through 7 minutes following application (TK, $P < .05$; Figure 4).

Pain in the no-saline/cryo condition increased during the first 2 minutes of application (TK, $P < .01$) but there were no differences from the previous pain measure from 3 minutes during application through the 10-minute postapplication phase (TK, $P > .14$).

Subjects were aware a needle was inserted deep to their patellar tendon, but they did not experience a level of pain that caused them to discontinue the study. In addition, no subject reported pain 24 hours following the investigation.

3.2 Temperature and thermocouple uncertainty

Surface temperature data are summarized in Table 1. There was a significant interaction between condition and time for surface temperature ($F_{4,99} = 25.84$; $P < .0001$). Patella and popliteal preapplication temperature between the 3 conditions remained constant (patella: TK, $P > .32$ and popliteal: TK, $P > .1$). Patella and popliteal fossa temperature for the 2 cryotherapy conditions were not different during application and postapplication (patella: TK, $P > .29$; popliteal: TK, $P > .1$). However, mean temperatures for the application and postapplication phases for the 2 cryotherapy conditions were less than means for the respective phases in the saline/sham condition

(TK, $P < .0001$). Patella and popliteal surface temperature did not change between phases for the saline/sham group (TK, $P > .6$). Ambient temperature fluctuated less than 1°C during data collection.

The thermocouples used to measure patella and popliteal fossa temperature displayed the same temperature readings in a room-temperature water bath before and after data collection. Thermocouple uncertainty for the patella and popliteal fossa were the same (± 0.05°C). Thermocouple uncertainty for ambient air was ± 0.04°C.

4. Discussion

Sterile 5% hypertonic saline intermittently infused into the infrapatellar fat pad produced fairly constant anterior knee pain that persisted for 20 minutes. Thus this pain model seems to be effective for investigating the effectiveness of therapeutic modalities used in conjunction with rehabilitation and skeletal muscle recruitment during and following anterior knee pain.

Single 0.2-0.25 cc injections of 5% hypertonic saline causes chemical irritation of the infrapatellar fat (Bennell et al., 2004). As a result, pain gradually increases during the first few minutes after injection, peaks at approximately 3 minutes, and then decreases to no pain around 15 minutes (Bennell et al., 2004). From preliminary investigations, increasing the injection quantity four fold (1 cc) resulted in similar published results (Bennell et al., 2004). However, by using different rates and volumes of continuous or intermittent infusion (Table 2) we were able to induce consistent pain for extended periods of time.

Using an established constant infusion pain model (Graven-Nielsen et al., 1997) resulted in intolerable pain which required subjects to discontinue their participation within 5 minutes of infusion. We also observed that different unpublished constant infusion methods tested in our laboratory, did not cause pain for 20 minutes (Table 2). During intermittent infusion, we noticed that subjects experienced constant pain during a 3-minute pause between subsequent infusions. The first intermittent infusion method tested, however, caused a significant amount of pain during the first infusion but pain decreased rapidly following subsequent infusions (Table 2).

Hypertonic saline stimulates nociceptors (Alessandri-Habner et al., 2005). Knowing how long these receptors remain activated however is unknown. From our data it is apparent that a constant level of pain can be maintained through intermittent infusion of 5% hypertonic saline.

Cryotherapy decreased pain within the first minute of application. This decrease possibly occurs through cold induced changes in receptor sensitivity (Kunesch et al., 1987), discharge rate of receptors(Wexler and Mayer, 1973), and/or supraspinal activity (Gordon and Heath, 1986; Di Piero et al., 1994; Watanabe et al., 1996; Casey et al., 2000). When skin surface temperature decreases below 10°C, peripheral receptor function becomes temporarily impaired during and following cold application (Kunesch et al., 1987). This impairment was likely due to receptor desensitization as a result of the cold. Subjects could not perceive painful sensations for up to 5 minutes following a 5-minute cold application (Kunesch et al., 1987). Since our skin surface temperatures were

below 10°C (Table 1), it is likely that the decrease in pain caused by hypertonic saline occurred as a result of receptor desensitization.

The differential response to cold in the saline/cryo and no-saline/cryo groups is interesting. The saline/cryo group experienced an immediate decrease in pain after 1 minute of cold application and the no-saline/cryo group experienced an increase in pain (Figure 2). These data support our clinical observation that cold application decreases pain in patients with orthopedic injuries (Airaksinen et al., 2003; Bleakley et al., 2004; Koç et al., 2006). and increases pain in subjects not experiencing injury pain (i.e. cold-induced pain) (Havenith et al., 1992). Cold-induced pain theories have been reviewed elsewhere (Knight, 1995).

Another interesting observation was the elevated pain measure at the minute 5 during hypertonic saline infusion for the saline/cryo group as compared to the saline/sham group. Uncontrollable variables such as anticipation (Fillingim and Maixner, 1995; Dao and LeResche, 2000), attitude towards the pain stimulus (Fillingim and Maixner, 1995; Dao and LeResche, 2000), stress (Fillingim and Maixner, 1995; Dao and LeResche, 2000; Bencherif et al., 2002), anxiety (Fillingim and Maixner, 1995; Dao and LeResche, 2000), or conscious awareness of knowing ice bags were going to be applied, may have added variability in the pain measures.

As expected, there was no difference in cooling for the no-saline/cryo and saline/cryo group. Cryotherapy decreased surface temperature at the center of the patella and popliteal fossa during application and increased during postapplication. Our surface temperature results from the sham application disagrees with the results observed in a

previous study.(Hawkins et al., 2007) A cat litter bag secured with a double length 6 inch ACE® wrap to the thigh muscles withdrew heat from the body. In our saline/sham group there was no difference in surface temperature when the cat litter bag was secured to the anterior and posterior knee joint (Table 1). Therefore, the location of the cat litter bag or the amount of compression may be responsible for these differences.

Our study was limited to the infrapatellar fat pad and 5% hypertonic saline. A previous investigator reported the pain arising from the infrapatellar fat pad may be beneficial in examining pain arising from the anterior knee (Bennell et al., 2004). The fat pad is innervated by the posterior articular nerve (Kennedy et al., 1982) a mixed (sensory and motor) nerve that also innervates the posterior knee joint capsule, cruciate ligaments, and menisci (Kennedy et al., 1982; Johansson et al., 1991). Other investigators examining pain arising from the anterior knee reported pain relief when a local anesthetic or steroid was injected into the infrapatellar fat pad (Tsirbas et al., 1991). In essence, the infrapatellar fat pad is a good location for studying pain arising from the anterior knee.

This pain model is based on the assumption that anterior knee joint pain caused by intermittent infusion of 5% hypertonic saline is similar to orthopedic related pain. This assumption is supported by another investigator who suggest that pain associated with decreases in motor function caused by 5% hypertonic saline are similar to those experiencing injury pain (Zedka et al., 1999).

5. Conclusion

Pain caused by intermittent infusion of 5% hypertonic saline is effective in producing a constant level of pain. Cryotherapy immediately decreases induced pain

within the first minute of application with a gradual decline during application. This experimental pain model may be useful in examining the effectiveness of various therapeutic interventions on pain and the effects of pain and cryotherapy on skeletal muscle recruitment.

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Table 1. Average patella and popliteal surface temperature during each application phase for each condition (n = 30 subjects; mean ± SD)

Location/Phase	Saline/cryo[*]	No-saline/cryo[†]	Saline/sham
Patella			
Preapplication	28.3 ± 1.1	27.7 ± 1.6	28.0 ± 1.2
Application[‡]	7.2 ± 4.5	6.7 ± 4.2	28.2 ± 1.1
Postapplication[‡]	10.9 ± 2.3	11.5 ± 2.4	28.3 ± 1.5
Popliteal			
Preapplication	32.8 ± 0.7	31.7 ± 1.9	32.6 ± 1.2
Application[‡]	8.4 ± 4.6	7.4 ± 4.2	32.4 ± 1.3
Postapplication[‡]	17.7 ± 3.9	18.5 ± 4.3	33.0 ± 1.3[§]

[*]Application < postapplication & preapplication. Postapplication < preapplication

[†]Application < postapplication & preapplication. Postapplication < preapplication

[‡]Saline/cryo & no-saline/cryo < saline/sham

Table 2. Infusion techniques tested and the duration of perceived pain

Infusion type	Pain duration
Constant infusion	
0.5 ml for 20 s, 2.2 ml for 440 s, 4.4 ml for 440 s*	Intolerable pain at 4 min into infusion
0.5 ml for 20 min†	Intolerable pain at 5 min into infusion
0.54 cc/min for 3 min, 0.1 cc/min for 17 min	Pain lasted 14 min
0.54 cc/min for 5 min, 0.1 cc/min for 15 min	Pain lasted 14 min
Intermittent infusion	
0.54 cc for 5 min, nothing for 3 min, 0.54 cc for 5 min, nothing for 7 min	Pain lasted 16 min
0.54 cc for 3 min, nothing for 3 min, 0.54 cc for 3 min, nothing for 3 min, 0.54 cc for 3 min, nothing for 3 min, 0.54 cc for 3 min, nothing for 3 min, 0.54 cc for 1 min	Pain lasted over 20 min

*modeled after infusion into the tibial anterior(Graven-Nielsen et al., 1997)

†modeled after infusion into erector spinae at L_3 level(Thunberg et al., 2005)

Figure 1. Teflon catheter inserted into the infrapatellar fat pad from the lateral side of the knee. The catheter was inserted perpendicular to the patellar tendon. In order to minimize interface temperature beneath the popliteal fossa we made a custom plastic bottle so that air could pass freely over the thermocouple sensing tip.

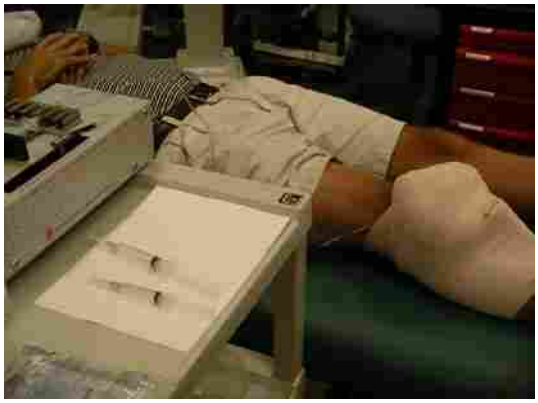


Figure 2. Set-up for the saline/cryo and sham groups. The two 1-kg bags were applied to the anterior and posterior surface of the knee joint.

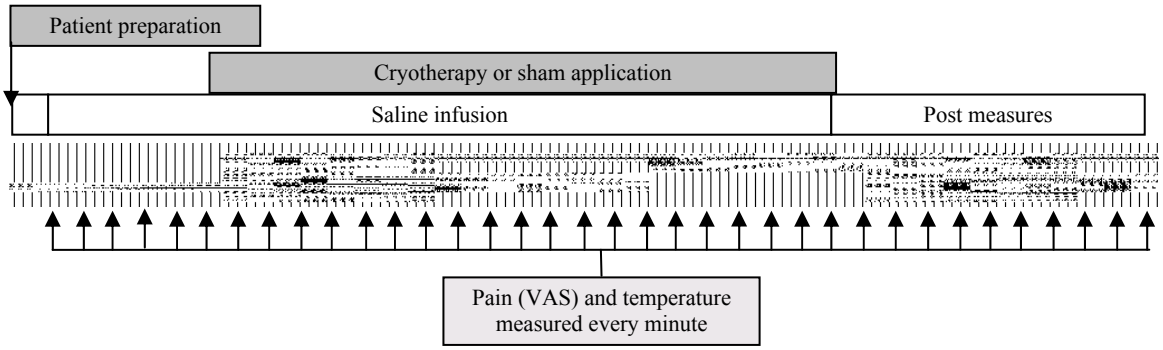
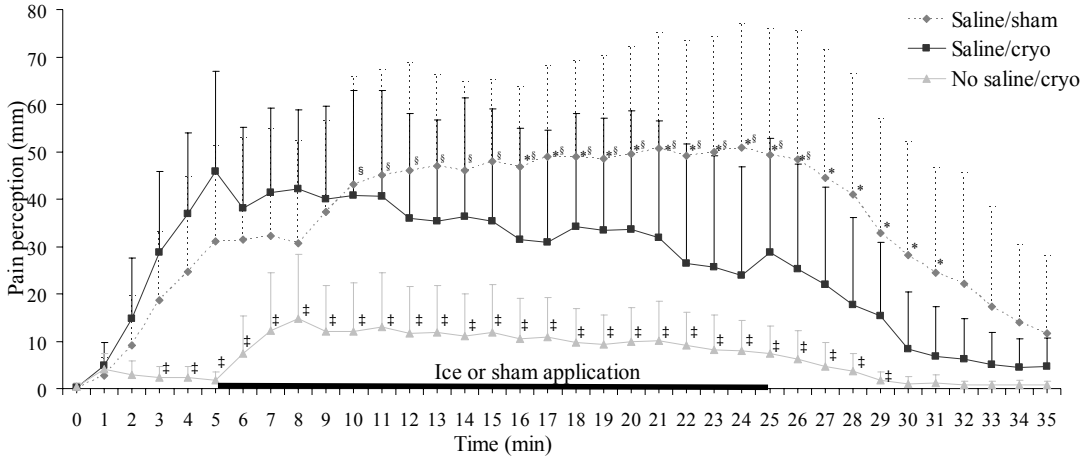


Figure 3. Timeline for data collection.



*Saline/sham > Saline/cryo (TK, $P < .05$)
†Saline/cryo > Saline/sham (TK, $P < .05$)
‡Saline /cryo > No-saline/cryo (TK, $P < .05$)
§Consistent pain for the Saline/sham condition (TK, $P < .05$)

Figure 4. Perceived pain for each condition across time. Each pain measure was recorded on new VASs every minute during data collection (preapplication = 6, application = 20, postapplication = 10; mean ± SD).

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Arthrogenic muscle inhibition occurs with pain and removed with cryotherapy

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ABSTRACT

Context: Clinically it is assumed pain contributes to arthrogenic muscle inhibition. Cryokinetics, a rehabilitation technique involving cold application and exercise, is suggested to facilitate exercise by reducing pain and arthrogenic muscle inhibition.

Objective: Determine if experimentally induced anterior knee pain contributes to arthrogenic muscle inhibition and if cold application influences either pain or arthrogenic muscle inhibition.

Design: A randomized controlled laboratory study.

Setting: Laboratory.

Participants: Forty physically active, healthy male participants (age=21.8±2.2yrs, ht=176.3±26.9cm, mass=75.96±8.7kg) volunteered.

Main Outcome Measure (s): H_{max}, M_{max}, McGill pain questionnaire, visual analogue scale (pain perception), and patella, popliteal, and ambient air temperature were measured.

Results: Pain resulted in arthrogenic muscle inhibition immediately following and 30 minutes following intermittent hypertonic saline infusion ($P<.0002$). Cryotherapy removed inhibition immediately following ($P<.0001$), but not 30 minutes following application ($P<.87$). Pain for the 3 saline infusion groups increased immediately following infusion as measured with the pain rating index ($P<.0001$) and visual analogue scale ($P<.0001$). According to pain rating index, cryotherapy did not decrease pain following ($P>.18$) or 30 minutes following application. Pain caused by saline infusion and cryotherapy were also higher than no-saline at 30 minutes following ($P<.008$).

Unlike the pain rating index, cryotherapy decreased pain following (P<.0001) and 30 minutes following application (P<.002) with the visual analogue scale. At 30 minutes following infusion, pain caused by cryotherapy and sham application were higher than no-saline (P<.04). Cryotherapy decreased temperature more than no cryotherapy (P<.0001).

Conclusions: Arthrogenic muscle inhibition occurred with anterior knee pain. A knee joint cryotherapy treatment disinhibited the quadriceps motoneuron pool and reduced pain as measured with visual analogue scales. Cryotherapy did not decrease pain as measured with the pain rating index.

Keywords: Pain, Cryotherapy, Hoffman reflex, Arthrogenic Muscle Inhibition

INTRODUCTION

Inhibition is one of the regulatory processes of the neuromuscular system.[1] One type, arthrogenic muscle inhibition (AMI), is a reflex inhibition of the musculature surrounding a joint that occurs following knee joint effusion[2, 3] or damage to the structures of that joint.[4, 5] It is reported that AMI is a limiting factor in joint rehabilitation, as it restricts skeletal muscle activation resulting in muscle weakness and muscle atrophy.[1, 4]

Pain, another factor affecting joint rehabilitation could contribute to AMI.[6] Examining pain and AMI in patients is problematic because of injury variability and patient subjectivity. Injured patients often have pain intensities that fluctuate in severity and may include other pathologies associated with joint injury thus making it difficult to quantify.[7] However, the recent development of an experimental joint pain model involving intermittent infusion of 5% hypertonic saline into the infrapatellar fat pad would alleviates some of the previously uncontrollable variables associated with injury related pain.

Cryokinetics is a rehabilitation technique that involves cold application and exercise. It is advocated that cold application facilitates the exercise by reducing pain and AMI.[8-10] It is also suggested that cryotherapy removes AMI and facilitates quadriceps motoneuron pool recruitment in subjects not experiencing pain.[2] No investigator, however, has examined if knee joint pain, independent of other factors and cryotherapy alters quadriceps motoneuron pool recruitment.

To evaluate quadriceps motoneuron pool recruitment and cryotherapy in the presence of knee joint pain, we asked the following research questions: 1) does pain induced by intermittent infusion of 5% hypertonic saline into the infrapatellar fat pad cause AMI and 2) does the combination of cryotherapy with intermittent infusion of 5% hypertonic saline alter involuntary motoneuron pool recruitment?

METHODS

Study Design

A 4 x 56 (treatment x time) randomized controlled laboratory study with repeated measures on time guided this study. Independent variables were treatment (saline infusion (saline), saline infusion/cryotherapy (saline/cryo), saline infusion/sham (saline/sham), and no-saline infusion (no-saline)) and time (pretreatment (pre), immediate posttreatment ($post_{tx}$), and 30-minutes posttreatment (30 min $post_{tx}$)). Measured dependent variables were H_{max}, M_{max}, McGill Pain Questionnaire (MPQ), and pain perception (visual analogue scale; VAS). Additionally, to ensure the temperature remained constant in the noncryotherapy treatment and to know the level of cooling in the saline/cryo treatment, patella and popliteal surface temperatures were measured every minute during preapplication, application, and postapplication.

Subjects

Sixty-seven physically active, male subjects were screened for this study. Of the 67 subjects, 27 (40%) were excluded because a measurable H_{max} and/or M_{max} measure could not be obtained. Therefore, 40 subjects (age = 21.8 ± 2.2 yrs, ht = 176.3 ± 26.9 cm, mass = 75.96 ± 8.7 kg) participated in this study. Each subject filled out a

preparticipation health history questionnaire to ensure that they were free of any lower extremity orthopedic, neurological, cardiovascular, and endocrine conditions before signing the approved institutional review board consent document.

Subjects then went through a 30-minute orientation and screening session. Orientation included an explanation of the experiment, including the risks and benefits of the study. Screening consisted of making sure subjects had a measurable maximum quadriceps H-reflex and M-response. Subjects who had the measurable responses were instructed on how to use the MPQ and VAS scales and rescheduled to return back to the laboratory 48 to 72 hours from the screening day for testing.

Instruments

Skin was debrided with skin prepping gel (Nuprep, D.O. Weaver & Co., Aurora, CO). H-reflex measures were collected using a stimulus isolation adaptor (STMISOC, BIOPAC Systems, Inc., Santa Barbara, CA) connected to a shielded bar electrode (EL503, BIOPAC Systems, Inc., Santa Barbara, CA) to deliver stimuli. Surface pregelled Ag-AgCl self-adhesive disk electrodes (EL 503-10; BIOPAC Systems, Inc., Goleta, CA) separated from each other by 2 cm were applied to the vastus medialis muscle. Signals from the surface electrodes were amplified with a Telemetry unit (TEL100M, BIOPAC Systems, Inc., Santa Barbara, CA) and further processed with a BIOPAC EMG system (MP150, BIOPAC Systems, Inc. Santa Barbara, CA). Input impedance of the amplifier was 2.0 MΩ, with a common mode rejection ratio of 110 dB, a signal/noise ratio of 65 dB, and a gain of 1000. Raw data were bandpass filtered at 10

and 500 Hz. A laptop computer was connected to the EMG system to map all H- and M_{max} measures.

Pain was induced with an implanted 24 gauge x 0.75 in (0.7 x 19 mm) Teflon catheter (Alliance Medical, Russellville, MO) or implanted Teflon catheter with simultaneous infusion of sterile 5% hypertonic saline (B. Braun Medical, Inc., Irvine, CA). To infuse saline, a 36 cm saline extension set (B. Braun, Medical Inc, Bethlehem, PA) was interfaced between the implanted Teflon catheter and a 5 cc syringe filled with 5% hypertonic saline. The syringe was positioned in a constant infusion pump (Harvard Apparatus, Millis, MA; model # 975) used to intermittently deliver saline for 20 minutes. Infusion rate was 0.54 cc a minute during 4 consecutive on/off cycles. The on/off cycles were 3 minutes with an exception of the last 2 minutes being "on." Total volume of saline infused was 5.94 cc. Once the first 5 cc syringe was infused a second 5 cc syringe filled with hypertonic saline was used.

Pain perception measures were taken with a MPQ and a 100 mm VAS. The MPQ is reported to be a reliable and valid tool when assessing the multi-dimensional perspective of pain.[11] The VAS was labeled "no pain" on the left polar end and "unbearable pain" on the right polar end.[12] When measures are taken every minute, the VAS is reported to be reliable tool in assessing pain ($r = 0.87$).[13]

Surface temperature was measured with three, PT-6 Kapton insulated thermocouples (Physitemp Instruments, Inc., Clifton, NJ) interfaced to 3 channels in a 16-channel Iso-Thermex electrothermometer (Columbus Instruments, Columbus, OH). A plastic bottle with a hole on each end and in the center was positioned on a pillow in the

popliteal fossa to minimize interface temperature between the popliteal fossa and the pillow (Figure 1) during baseline and postapplication measures. All temperature data were stored in a desktop computer interfaced to the Iso-Thermex electrothermometer. Temperatures were recorded every minute throughout data collection.

Testing Procedures

Subjects reported to the laboratory dressed in shorts and a T-shirt. They completed a MPQ and VAS before being randomly assigned to 1 of the 4 treatments. Subjects filled out the pain scales before their random assignment because knowing what treatment they were assigned to, may have influenced the words selected on the MPQ.

Subjects were again screened to ensure they had the H-reflex and M-response measures. In order to perform the screening and H-reflex and M-response measures, a 6 X 6 cm area over the greatest bulk of the vastus medialis and a 3 x 3 cm area over the tibial tuberosity were shaved and debrided for EMG electrode application on the dominant leg (ie, leg with which they kick a ball). Two electrodes were applied to the greatest bulk of the vastus medialis as found during a maximal voluntary isometric contraction to eliminate crosstalk between adjacent muscles. A ground electrode was placed on the tibial tuberosity to eliminate noise. Electrodes were placed 2 cm center to center and inline with the longitudinal axis of the muscle. The stimulus electrode was then placed over the femoral nerve in the femoral triangle. To locate the nerve, the femoral pulse was first located. The electrode was placed just lateral to the pulse where the nerve is located. Next, in order to find the best location over the nerve, a series of stimuli were delivered in order to find an H-reflex and M-response.

Subjects were positioned prone on a treatment table where a 3 x 3 cm area in the center of the popliteal fossa was shaved and cleansed with 70% isopropyl alcohol for thermocouple application. Following application, subjects were positioned supine with their dominant leg bent to approximately 15° of knee and hip flexion. A 3 X 3 cm area over the patella was shaved and cleansed with 70% isopropyl alcohol for thermocouple application and a 3 X 3 cm area immediately lateral to the patellar tendon was shaved for catheter needle insertion.

The stimulus electrode was then fixed to the femoral nerve with transdermal tape and 2 double length 6-inch elastic wraps. One of the elastic wraps was unrolled and placed on top of the stimulating electrode. The second elastic wrap was wrapped around the subjects' hips to compress the unrolled ace wrap into the stimulus electrode (Figure 1).

Subjects then placed their foot in a polystyrene cube, designed to keep the heel stable and the lower extremity in a fixed position. They placed their hands to their sides with their palms up and hands open, focused at a small picture on the ceiling, and listened to a constant auditory sound (*i.e.* white noise) through headphones (Figure 1). These steps were performed to decrease potential variability in the measures and to assist in reliability.[14]

A series of short duration, high intensity stimuli were delivered through the stimulus electrode with varying amplitudes (2-5 mA increments) in order to find the maximum H-reflex (H_{max}). With the stimulating amplitude set at H_{max}, 5 measures were recorded with a 20-second rest between measures. The stimulus intensity was then

gradually increased to find the maximum M-response (M_{max}) for H-reflex normalization. Once the M_{max} was identified, 5 measures were recorded with a 20-second rest between measures.

Once H- and M_{max} measures were taken, the catheter insertion site was cleansed with povidone-iodine solution for needle insertion. In order to find the infrapatellar fat pad, the lateral border of the patellar tendon was located through palpation (Figure 2). The catheter needle was then inserted deep to the patellar tendon and distal to the patella to a depth of 19 mm. Once inserted, the needle was extracted leaving the flexible Teflon catheter implanted in the infrapatellar fat pad (Figure 3).

For the saline/cryo or saline/sham treatments the saline extension set was interfaced between the implanted catheter and 5 cc syringe positioned in the infusion pump. The pillow and plastic bottle was removed from the posterior side of the knee joint and two 1-kg bags of crushed ice or cat litter (sham bags) were secured to the knee joint with a double 6-inch elastic wrap during the 20 minutes of intermittent infusion. One bag was applied to the anterior surface and the other to the posterior surface. Care was taken so the bags did not come in contact with the electrodes. For the saline-only treatment the extension set was also interfaced between the implanted catheter and 5 cc syringe positioned in the infusion pump. These subjects however did not receive treatment or intervention during the 20 minutes of intermittent infusion. The no-saline treatment only received the implanted Teflon catheter. The catheter remained in place for the same length of time as the 3 saline infusion treatments.

At minute 19, during treatment and minute 29 following treatment, subjects were given a blank MPQ and VAS and instructed to read the 20 boxes of words in order to reacquaint themselves with the MPQ. At minutes 20 and 30, subjects selected the words on the MPQ that represented their perceived pain and placed a vertical line on the VAS before receiving another set of H_{max} and M_{max} measures.

Immediately following data collection, the Teflon catheter was extracted from the infrapatellar fat pad and the insertion site was treated with antibiotic ointment and a Band-Aid.

Statistical Analysis

Means and standard deviations were computed for H:M_{max} ratio, pain rating index (PRI), VAS, and patella, popliteal, and ambient temperature pre, immediate $post_{tx}$ and 30 minute $post_{tx}$. The mean of 5 H_{max} and 5 M_{max} measures were used to calculate a quadriceps H:M_{max} ratio. Percent changes in H:M_{max} ratio were also calculated. The PRI was calculated by summing the numerical value for each word selected in the sensory, affective, evaluative, and miscellaneous sections of the MPQ. Pain perception scores on the VASs were measured in millimeters from the left polar end.

Six 3 X 4 (time X treatment) mixed model analyses with repeated measure on time for subjects were used to examine differences in the H:M_{max} ratio, PRI, VAS, patella and popliteal surface temperatures, and ambient air temperature.

Tukey-Kramer post hoc multiple comparison tests were used to examine individual differences in perceived pain and temperature between treatments at each time. For all differences, the level of significance was set at $P < .05$. Data were analyzed with

the MIXED procedures of Statistical Analytical Software (SAS; 9.1 Carey, North Carolina).

Thermocouple uncertainty (validity + reliability) was computed for the 3 thermocouples according to Jutte et al.[15, 16]

RESULTS

H:M_{max} ratio

There was a significant time by treatment interaction for the H:M_{max} ratio ($F_{6,72}$ = 13.12; $P < .0001$). These interactions are summarized in Figure 5. Percent change in H:M_{max} ratio over time are presented in Figure 6.

Pain caused by saline infusion alone and saline infusion with sham ice bag (cat litter) application resulted in AMI immediately following and 30 minutes following infusion (TK, $P < .0002$). Cryotherapy removed inhibition immediately following (TK, $P < .0001$) but not at 30 minutes following application (TK, $P < .87$). Pain caused by the implanted Teflon catheter did not cause AMI (TK, $P > .79$).

Pain perception

There were significant time by treatment interaction for the PRI ($F_{3,36}$ = 6.1; P = .002) and VAS ($F_{3,36}$ = 13.85; $P < .0001$). These interactions are summarized in Tables 1 and 2. The reported pain measures on the PRI were different than the VAS.

Pain rating index – Pain for the 3 saline infusion groups increased immediately following infusion (TK, $P < .0001$). Cryotherapy did not decrease pain immediately following application (TK, $P > .18$) or 30 minutes following application as compared to the saline/no cryo treatment. Pain caused by saline infusion and cryotherapy application

was higher than no-saline 30 minutes following application (TK, $P = .008$). Pain caused by the implanted Teflon catheter was not different than saline alone and saline sham application 30 minutes following infusion (TK, $P > .09$).

Visual analogue scale – Pain for the 3 saline infusion groups increased immediately following infusion (TK, $P < .0001$). Unlike the PRI, cryotherapy decreased pain following (TK, $P < .0001$) and 30 minutes following application (TK, $P < .002$) as compared to the saline/no cryotherapy treatment. At 30 minutes following application pain caused by cryotherapy and sham application were higher than no-saline (TK, $P < .04$). Pain caused by the implanted Teflon catheter was not different than saline infusion alone at 30 minutes following infusion (TK, $P < .23$).

Temperature & thermocouple uncertainty

There was a significant time by treatment interaction for patella ($F_{6,72} = 343.2$; $P < .0001$) and popliteal ($F_{6,72} = 205.9$; $P < .0001$) surface temperature. These interactions are summarized in Table 3.

As expected, cryotherapy decreased temperature more than no cryotherapy immediately following and 30 minutes following application (TK, $P < .0001$). Temperature did not change for the noncooling groups (TK, $P > .17$).

There was no difference in ambient air temperature between groups across time ($F_{6,72} = 0.75$; $P = .61$). Temperature fluctuated less than 1°C across time.

Thermocouples used to measure both patella and popliteal fossa temperature were displayed the same temperature recordings in a room-temperature water bath before and

after data collection. Thermocouple uncertainty for the patella and popliteal fossa were the same (± 0.05°C). Thermocouple uncertainty for ambient air was ± 0.04°C.

DISCUSSION

This study supports clinical observations that AMI occurs in subjects experiencing anterior knee pain[6] and extends the observations that knee joint effusion is not the only contributing factor to quadriceps AMI. It appears that pain in the absence of joint effusion results in AMI. In addition, the use of a 20-minute cryotherapy treatment decreases pain (as measured with a VAS), removes AMI associated with pain, and facilitates the quadriceps motoneuron pool beyond baseline measures.

These results disagree with the conclusion that pain and cryotherapy do not influence motoneuron pool recruitment in patients with patello-femoral dysfunction (PFD).[17] The major differences between what was reported and our study are type of pathology, sample size, level of perceived pain prior to treatment, and location and length of cold application. In the previous study[17], PFD related pain was likely initiated by other inflammatory mediators. Pain caused by our experimental pain model, however, appears to be caused by nociceptor stimulation.[18] In addition, the previous study had a low statistical power, we however, had a high statistical power ($\beta = 1.0$). This is likely due to the sample size taken or variations in pain between subjects. It is likely that those patients experiencing PFD had fluctuations in pain. These fluctuations in pain were likely greater than our induced pain because we controlled for the observed pain. In both investigations cryotherapy decreased pain following application as measured with VASs, but the specific level of pain prior to application was not reported. In addition, the

location and length of cold applications were different. A single ice pack was applied to the anterior surface of the knee joint for 10 minutes. [17] We simultaneously applied 2 ice bags to the knee joint for 20 minutes. This application time is more commonly used for joint rehabilitation.[8, 9]

Some suggest that pain, which often accompanies joint trauma, contributes to AMI.[6, 9] Until now, however, there have been no data that specifically focused on the contribution of pain to AMI. Previous work examining quadriceps AMI has been limited to the changes associated with joint trauma following orthopedic surgery[4, 5] and an artificial knee joint effusion model.[2, 3] In the studies examining AMI following surgery, factors such as effusion, pain, inflammation, and atrophy may have contributed to the AMI. Those who specifically focused on knee joint effusion, reported an approximate 25% decrease in motoneuron pool recruitment.[2, 3] These data are comparable to the 37% decrease following pain associated with intermittent infusion of 5% hypertonic saline (Figure 6). Additional data are needed to determine the relative contribution of pain and other consequences of joint trauma and healing.

Arthrogenic muscle inhibition is thought to occur through pre-[19] and post-synaptic mechanisms.[19, 20] Observations, which were made using a joint effusion model, may or may not relate to mechanisms associated with experimentally induced anterior knee pain. Experimentally induced anterior knee pain may cause quadriceps AMI through pre- or post-synaptic mechanisms, mediated by supraspinal centers and/or interneuronal mechanisms at the spinal cord. However, the pain stimulus likely activated a separate set of receptors and interneurons associated with the sensory input following knee joint

effusion. Regarding supraspinal activity, it is known that joint afferents are under tonic descending inhibitory control.[21] However, knowing which supraspinal regions are involved with AMI in the presence of pain remains unknown.

Cryotherapy disinhibited and facilitated the quadriceps motoneuron pool. These changes in motoneuron pool activity may have been caused by decreased receptor threshold[22] and/or supraspinal activity.[23-26] Applying ice bags to the knee joint activates mechanoreceptors (pressure from the ice bag)[27] and thermoreceptors (decreases in tissue temperature).[28] By activating both types of receptors, information conveyed to or from the spinal cord and supraspinal centers may influence quadriceps motoneuron pool excitability. It is likely that cooling is a cause of disinhibition and facilitation since pressure from the sham ice bag (cat litter) did not result in quadriceps facilitation (Table 3). Additional research is needed to determine if thermoreceptors alone or the combined activation of thermoreceptors and mechanoreceptors are involved in quadriceps motoneuron pool recruitment.

Differences between pain perception as measured by the VAS and MPQ are likely due to differences in the philosophies of the two scales. The VAS measures the intensity of pain.[29] The MPQ on the other hand, is a comprehensive pain-measure tool that measures (ie sensory, affective, evaluative, and miscellaneous) aspects of pain.[30] The MPQ was developed to evaluate the pain experiences of patients suffering from chronic pathologies.[30] We used it to see if it would be beneficial in this situation. It appears that the MPQ may not be a useful pain measuring tool when examining cryotherapy and experimentally induced pain. When scoring the MPQ, words from 4 categories are

assigned a numerical value.[30] It is likely the words selected from the miscellaneous category were somewhat responsible for the observed difference between pain scales. This category, which allows subjects to select words such as "cold" and "cool", may have added variability to the overall pain score. Many investigators examining pain relief during a cryotherapy treatment used the VAS.[17, 31-34]

The clinical significance of this study was the beneficial effects of cryotherapy on pain and recruitment.[9] Clinicians should consider incorporating a cryotherapy treatment prior to therapeutic rehabilitation in helping minimize pain and facilitate knee joint exercise.

This study is limited because of the two assumptions regarding our motoneuron pool measurement technique and pain induction. The H-reflex is reported to be a reliable method when used to assess availability of motoneurons in the quadriceps motoneuron pool.[14] The measures, however, are taken at rest and do not account for supraspinal influences during voluntary movement. In addition the data were limited to the vastus medialis muscle in subjects who were physically active, who did not have a large amount of subcutaneous tissue overlying the femoral nerve.

This pain model is based on the assumption that anterior knee pain caused by intermittent infusion of 5% hypertonic saline is similar to orthopedic related pain. This assumption is supported by the observations that a reduction in motor function caused by saline induced pain is similar to patients experiencing injury pain.[35]

Experimental pain was induced in the infrapatellar fat pad with 5% hypertonic saline. Others reported pain arising from the infrapatellar fat pad may be beneficial in

examining pain arising from the anterior knee.[36] The fat pad is innervated by the posterior articular nerve[37] a mixed (sensory and motor) nerve that also innervates the posterior knee joint capsule, cruciate ligaments, and menisci.[37, 38] Other investigators examining pain arising from the anterior knee reported pain relief when a local anesthetic or steroid was injected into the infrapatellar fat pad.[39] In essence the infrapatellar fat pad is a good location for studying pain arising from the anterior knee.

CONCLUSIONS

Pain is a contributing factor to quadriceps AMI. A local 20-minute cryotherapy treatment removes the observed AMI and facilitates quadriceps motoneuron pool immediately following, but not 30 minutes following application. A 20-minute cryotherapy application decreases experimentally induced anterior knee pain as measured with the VAS but not with the MPQ-PRI.

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Table 1. Calculated PRI for each treatment across time. Measures include the average value for the sensory, affective, evaluative, and miscellaneous sections of MPQ (n = 10 measures/cell; mean ± SD)

Group	Pre	$Post_{tx}$[‡]	30 min $post_{tx}$[§]
Saline[*]	0.0 ± 0.0	17.1 ± 10.3	5.3 ± 6.2
Saline/cryo[†]	0.0 ± 0.0	12.2 ± 4.2	8.2 ± 8.2
Saline/sham[*]	0.0 ± 0.0	16.0 ± 7.7	5.1 ± 4.7
No-saline	0.1 ± 0.3	0.7 ± 1.1	0.4 ± 0.7

[*] $Post_{tx}$ > 30 min $post_{tx}$ & pre; 30 min $post_{tx}$ > pre

[†] $Post_{tx}$ and 30 min $post_{tx}$ > pre

[‡] Saline, saline/cryo, and saline/sham > no-saline

[§] Saline/cryo > no-saline

Table 2. Pain perception as measured on each VAS (n = 10 measures /cell; mean ± SD)

Group	Pre	$Post_{tx}$[†]	30 min $post_{tx}$[‡]
Saline[*]	0.0 ± 0.0	49.5 ± 23.7	8.4 ± 9.5
Saline/cryo[*]	0.0 ± 0.0	28.6 ± 7.7	12.1 ± 8.0
Saline/sham[*]	0.0 ± 0.0	45.5 ± 24.3	13.8 ± 13.8
No-saline	0.0 ± 0.0	0.7 ± 1.3	0.5 ± 0.9[‡]

[*] $Post_{tx}$ > 30 min $post_{tx}$ & pre; 30 min $post_{tx}$ > pre

[†] Saline & saline/sham > saline/cryo > no-saline

[‡] Saline/cryo & saline/sham > no-saline

Table 3. Patella and popliteal surface temperature (°C) for each treatment. Measures were taken the last minute during the 3 application phases (n = 3 measures/group; mean ± SD)

Group	Pre	$Post_{tx}$ [†]	30 min $post_{tx}$ [†]
Patella			
Saline	28.2 ± 1.1	28.1 ± 1.0	28.2 ± 1.1
Saline/cryo[*]	27.1 ± 1.9	10.5 ± 4.5	16.3 ± 4.0
Saline/sham	28.0 ± 0.9	27.9 ± 0.9	28.3 ± 1.2
No-saline	27.3 ± 1.0	27.5 ± 0.8	27.4 ± 0.5
Popliteal			
Saline	33.2 ± 0.7	30.5 ± 1.1	33.5 ± 1.6
Saline/cryo[*]	32.7 ± 0.9	6.9 ± 2.9	28.2 ± 1.7
Saline/sham	32.4 ± 1.0	32.4 ± 1.4	33.4 ± 0.9
No-saline	32.3 ± 1.1	33.6 ± 1.1	33.6 ± 1.0

[*] $Post_{tx}$ < 30 min $post_{tx}$ & pre; 30 min $post_{tx}$ < pre

[†] Saline/cryo < saline, saline/sham, & no-saline

Figures Legend

Figure 1. Set-up for the H_{max} and M_{max} measures

Figure 2. Teflon catheter insertion. Prior to insertion the lateral border of the patellar tendon was palpated. The catheter was then implanted deep to the patellar tendon.

Figure 3. Implanted Teflon catheter. Once the catheter was implanted a 5 inch piece of ½ in transdermal tape was used to secure and stabilize the catheter to the skin.

Figure 4. Timeline for data collection

Figure 5. H:M_{max} ratios for each treatment across time. Measures were taken pre, $post_{tx}$, and 30 min $post_{tx}$ for each of the 4 treatments (n = 10 subjects/group; mean ± SD) (n = 10 subjects/ group; mean ± SD)
*Pre > $post_{tx}$ & 30 min $post_{tx}$
†$Post_{tx}$ > pre & 30 min $post_{tx}$
‡Saline/cryo > saline & saline/sham
§No-saline > saline & saline/sham
$^{\|}$No-saline > saline & saline/sham

Figure 6. Percent change in H:M_{max} ratio across time. Percentages greater than 0 indicates facilitation; values less than 0 indicates AMI.

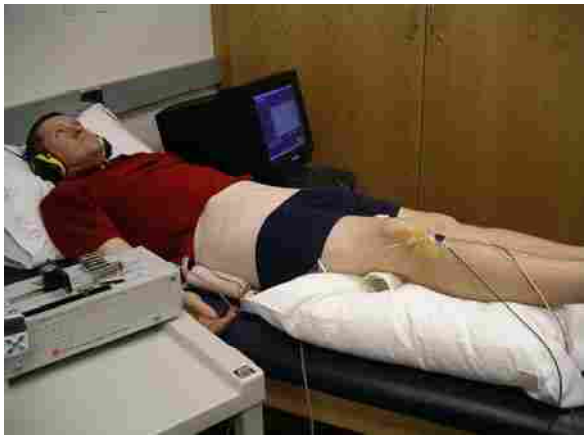


Figure 1.

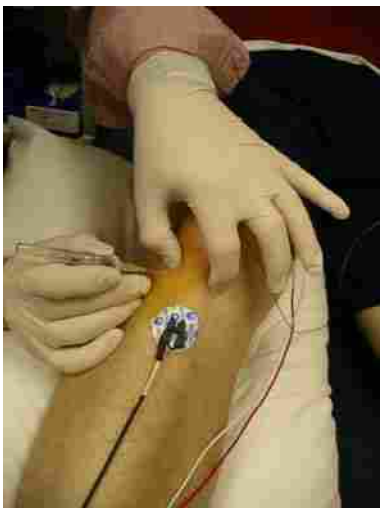


Figure 2.

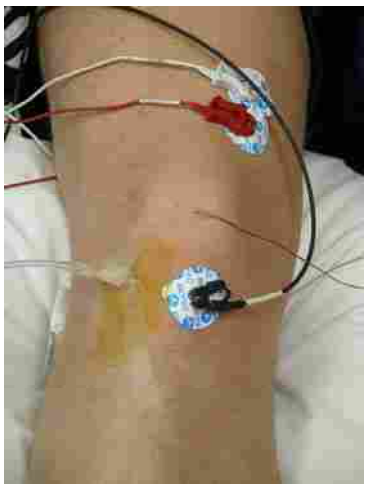
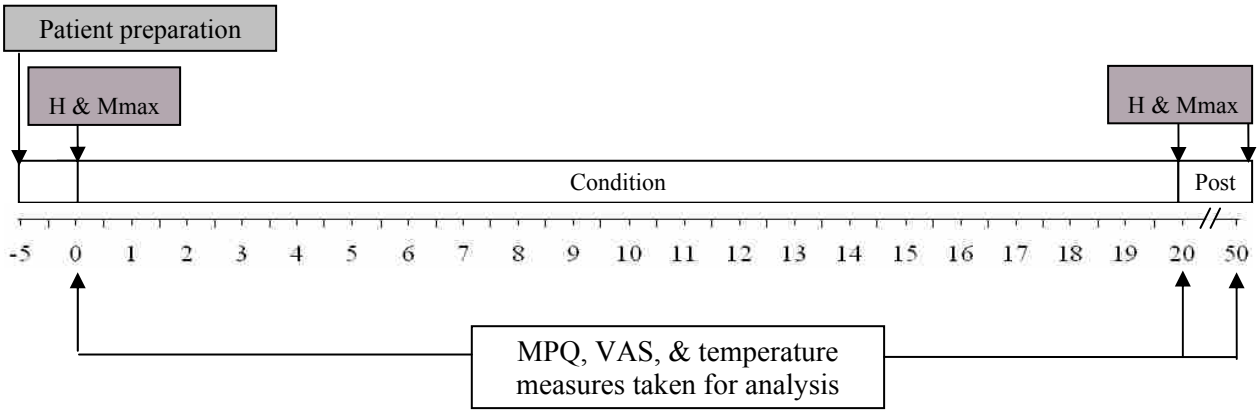


Figure 3.


Patient preparation
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H & Mmax
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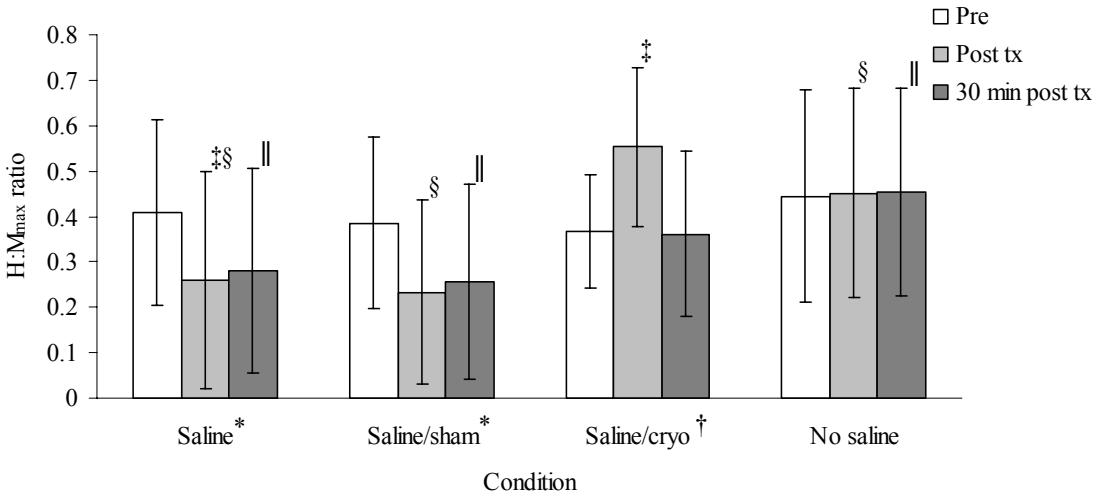
MPQ, VAS, & temperature measures taken for analysis

Figure 4.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Saline*
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Saline/cryo †
No saline
Condition

Figure 5.

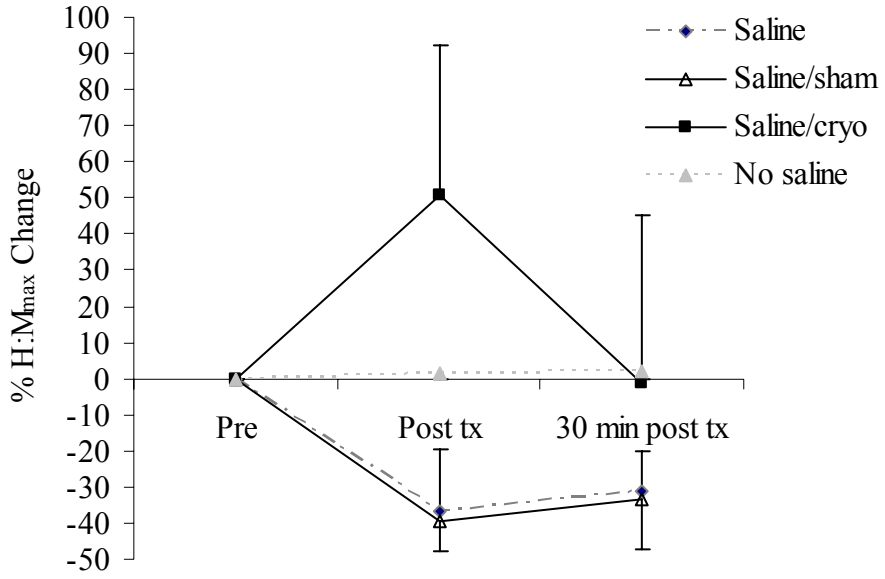
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Figure 6.

Appendix A

Prospectus

Chapter 1

INTRODUCTION

Cryotherapy is often used with rehabilitative exercise.[1-3] With cryotherapy, patients often perform exercises that were not possible prior to the cold application.[1] Some indicate that this enhanced ability is due to cold-induced pain reduction, which allows patients to begin rehabilitative exercises quicker.[1, 4-7] Others, however, report cryotherapy removes arthrogenic muscle inhibition (AMI) and facilitates motoneuron pool activation immediately following and 30 minutes following application in subjects not experiencing pain.[8-10] Therefore, cryotherapy may enhance exercise by facilitating skeletal muscle activation rather than, or in addition to reducing pain. No investigator, however, has examined if exercise is facilitated by cold in the presence of pain.

Arthrogenic muscle inhibition occurs when the musculature surrounding the knee joint shuts down following distension,[9, 11] and acute[12] or chronic[13, 14] joint pathology. Arthrogenic muscle inhibition occurs in the absence of pain;[9, 15, 16] for example, subjects receiving meniscectomies presented with AMI after pain subsided and following an injection of bupivacaine.[15, 16] In addition, injecting 60 cc of isotonic saline into the knee joint capsule of uninjured subjects causes AMI but not pain.[9, 11]

Investigating pain in injured patients is problematic because of patient subjectivity. Injured patients often have pain intensities that fluctuate in severity.[17] Many investigators have therefore, developed pain models by injecting or infusing 5% hypertonic saline into skeletal muscle. These pain models, however, cannot be used when investigating a 20-minute cryotherapy treatment and AMI.

Single injection of hypertonic saline produces mild to severe pain with a gradual onset and rapid decline in about 13 minutes following injection.[17] This pain model would be inadequate in examining a 20-minute cryotherapy treatment and AMI because pain caused by the injection would dissipate before the end of the treatment. Therefore, in order to solve this problem, a pain model that extends at least 20 minutes is needed.

Pain models involving infusion of 5% hypertonic saline over time have been suggested with various infusion rates and volumes.[18-21] Some involve short infusions lasting about 20 to 40 seconds[21-23] while others involve large volumes of 5% hypertonic saline infused for approximately 15 minutes.[19, 24] Through pilot work we noticed that these established pain models did not cause pain for at least 20 minutes or caused to much pain within the first 5 minutes of the infusion, thus subjects had to discontinue the study.

No investigator has reported a pain model that produces a fairly constant level of pain in a joint for 20 minutes. Such a pain model would allow investigators to examine the interaction between pain, cryotherapy, and AMI. The purpose of this investigation, therefore, is to establish the reliability of our pain model and examine how cryotherapy may influence AMI in the presence of pain. Specifically, the following research questions will be answered.

1. Does an intermittent infusion of 5% hypertonic saline into the infrapatellar fat pad cause consistent pain?

2. Does a 20-minute cryotherapy application during a 25-minute intermittent infusion of 5% hypertonic saline into the infrapatellar fat pad decrease pain?
3. Does a 20-minute intermittent infusion of 5% hypertonic saline into the infrapatellar fat pad cause AMI?
4. Does a 20-minute cryotherapy application with a 20 minute intermittent infusion of 5% hypertonic saline into the infrapatellar fat pad alter motoneuron pool recruitment?
5. Does a 20-minute sham ice bag application with a 20-minute intermittent infusion of 5% hypertonic saline into the infrapatellar fat pad alter pain?
6. Does a 20-minute sham ice bag application with a 20-minute intermittent infusion of 5% hypertonic saline into the infrapatellar fat pad alter motoneuron pool recruitment?

RESEARCH HYPOTHESIS

The following hypotheses will be tested:

1. An intermittent infusion of 5% hypertonic saline into the infrapatellar fat pad will cause consistent pain for 25 minutes.
2. A 20-minute cryotherapy application with a simultaneous 25 minute infusion of 5% hypertonic saline into the infrapatellar fat pad will decrease pain.
3. A 20-minute cryotherapy application with a simultaneous infusion of 5% hypertonic saline into the infrapatellar fat pad will cause AMI.

4. A 20-minute cryotherapy application with a simultaneous infusion of 5% hypertonic saline into the infrapatellar fat pad will facilitate motoneuron pool recruitment.
5. A 20-minute sham ice bag application with simultaneous infusion of 5% hypertonic saline into the infrapatellar fat pad will not decrease pain.
6. A 20-minute sham ice bag application with simultaneous infusion of 5% hypertonic saline into the infrapatellar fat pad will not decrease motoneuron pool recruitment?

DEFINITIONS OF TERMS

Arthrogenic Muscle Inhibition (AMI) – Ongoing reflex inhibition of the musculature surrounding a joint as observed with a decrease in H-reflex amplitude.[8]

Hoffman Reflex (H-reflex) – A monosynaptic reflex induced by stimulating a mixed peripheral nerve. It represents the motoneuron pool capable of being activated.

Motor Response (M-resposne) – Represents activation of the motoneurons located in the anterior horn of the spinal cord.[25]

H_{max} – Estimate of the number of motoneurons that are capable of activation as measured with the H-reflex[25]

M_{max} – Represents activation of the entire motoneuron pool as measured with the H-reflex.[25]

Motoneuron – An efferent fiber that innervates the polar regions of the muscle spindle.

Motoneuron Pool – Population of motoneurons that innervate a single muscle.

Resting Temperature – Skin surface temperature measurement after 5 minutes of no physical activity prior to the treatment.

Ice Bag – A plastic (polyethylene) bag filled with 1-kg of crushed ice with air removed.

Sham Bag – A plastic (polyethylene) bag filled with 1-kg of cat litter with air removed.

Physically Active – Subject who participates in aerobic activity for at least 2 hours a week.

Healthy – Subject who does not have a neurological, cardiovascular, endocrine, or orthopedic condition. In addition, the subject is not currently taking prescription or over-the-counter medications, diagnosed with an illness, or allergic to ice or latex.

Visual Analogue Scale – Pain scale measuring 100 mm in length with the indicators "no pain" on the left end and "unbearable pain" on the right end.[26]

McGill Pain Questionnaire – 20 groupings of 3 to 5 associated words. The 20 groupings are then divided into 4 subclasses, each of which measures one of the qualities of pain: Sensory pain (groups 1-10), Affective pain (groups 11 to 15), Evaluative pain (group 16), and Miscellaneous pain (groups 17 to 20).[27]

Experimental Pain – Infusion of 5% sterile hypertonic saline into the infrapatellar fat pad.

ASSUMPTIONS

This study will be based on the following assumptions:

1. Subjects will honestly answer questions on the pre-participation questionnaire.
2. Hoffman reflex (H-reflex) is an estimate of motoneuron pool excitability.
3. Maximum M-response (M_{max}) represents activation of the entire motoneuron pool of the vastus medialis muscle.

DELIMITATIONS

1. Cryotherapy will be a 1 kg crushed ice bag.
2. Sham bag will be a 1 kg cat-litter bag.
3. Subjects in Experiment 2 will have a measurable quadriceps H-reflex and M-response.
4. All subjects will be male volunteers.
5. All subjects will be free from neurological, vascular, or endocrine disorders.
6. All subjects will be free from any lower extremity pathology for the last year and never had lower extremity surgery.
7. All subjects will not consume caffeine at least 24 hours prior to testing.

8. All subjects will not be taking over-the-counter or prescription medication for pain or any other illness.

LIMITATIONS

1. The H-reflex is an induced reflex which does not occur naturally in the human body. The stimulus activates large diameter fibers before the small diameter fibers.
2. The quadriceps H-reflex measure can only be obtained in a limited population.
3. Five percent hypertonic saline is being used as a pain model to make conclusions about individuals experiencing pain following a musculoskeletal injury.

Chapter 2

REVIEW OF LITERATURE

Pain may limit a patient from being able to activate motoneurons. This limitation may lead to less compliant therapeutic rehabilitation sessions. Cryotherapy is beneficial in the transitional phase of therapeutic rehabilitation. It decreases perceived pain so that patients are able to begin their therapeutic rehabilitation sooner. In addition to decreasing perceived pain, cryotherapy may disinhibit and facilitate motoneuron pool activity during or following a painful stimulus. The purpose of this literature review is to describe the sensorimotor system, pain, motoneuron activity, and cryotherapy. Following are the topics included in this review.

- Cerebellum and Pain
- Vision, Vestibular, and Auditory Systems
- Descending Motoneurons
  - Upper Motoneurons
    - Medial Activation System
    - Lateral Activation System
  - Lower Motoneurons
- Efferent Pain Tracts

Pain

- Gender Differences in Pain
- Neurotransmitters and Pain
- Pain Theories
  - Specificity Theory
  - Von Frey's Theory
  - Pattern Theory
  - Gate Theory
  - Central Biasing Theory
  - Endogenous-Opiate Theory
  - Neuromatrix Theory
- Measuring Pain
  - Number Rating Scale
  - Graphic Rating Scale
  - Verbal Rating Scale
  - McGill Pain Questionnaire
  - Short-Form McGill Pain Questionnaire
  - Visual Analogue Scale
- Experimental Pain
  - Hypertonic Saline Administration
  - Hypertonic Saline and Involuntary Motor Output
  - Hypertonic Saline and Voluntary Motor Output

Inhibition

- Spinal Inhibitory Interneurons
  - Ia Inhibitory Interneurons
  - Ib Inhibitory Interneurons
  - Renshaw Cells

Measuring Motoneuron Activity

- Electromyography
- Hoffman Reflex
  - H-reflex and M-response
  - H_{max} and M_{max}
  - H:M_{max} Ratio
  - Subject Positioning
  - H-reflex Delivery

Voluntary Force Production

DATA BASES AND KEYWORDS SEARCHED

This review of literature was accomplished by using the following databases: National Library of Medicine's Pubmed (Medline) from the years 1966 to current, sport discus software (SPORTDiscus) from years 1975 to current, silver platter (CINHAL) from 1982 to current. Additional information was obtained from references cited and course textbooks. The following keywords were used:

Pain	Brain
Experimental pain	Cerebellum
Hypertonic saline	Basal Ganglia
Capsaicin	Somatosensorty cortex
Bradykinin	Primary motor cortex
Glutamate	fMRI imaging
Substance P	PET imaging
Serotonin	Vision
Endorphin	Auditory
Dynorphin	Neurotransmitter
Endomorphin	GABA
Pain scales	Prostaglandin
Inhibition	Electromyography
Recruitment	Interpolated twitch
Hoffman reflex	Central activation ratio
Anatomy	Voluntary contraction
Interneuron	Effusion
Vestibular	Gender differences
Knee	Cryotherapy
Soleus	Ice
Spinal cord	Perception

SENSORIMOTOR SYSTEM AND PAIN

The sensorimotor system consists of sensory, integration, and motor response of the neurological system.[28] This includes the detection of stimuli, conversion of stimuli to action potentials, and propagation of action potentials to integration regions of the spinal cord, brainstem, and brain. Following integration, descending motor responses are conveyed down the spinal cord and then to muscles in order to maintain joint homeostasis during functional activity.[28]

Sensory Afferent Nerve Receptors

Touch and Pressure (cutaneous) Receptors. Receptors activated by touch and pressure are called mechanoreceptors. Mechanoreceptors are nerve endings located in the superficial and deep layers of the skin. Five different touch and pressure mechanoreceptors include Meissner's corpuscles, Pacinian corpuscles, hair follicle receptors, Merkel's cells, and Ruffini endings.[29, 30]

Meissner corpuscles, Pacinian corpuscles, and hair follicle receptors are rapidly adapting receptors, meaning they respond to the initial application or removal of a stimulus but fail to respond during maintained stimulation. Meissner corpuscles (~30-40 μm in diameter) are located within the superficial epidermal layer of the skin. They are activated with light touch and vibration. Pacinian corpuscles (~100-500 μm in diameter) are located within the deep epidermal layer of the skin. They respond to rapid pressure placed on the skin and deep rapid vibrations moving across the skin. Hair follicle receptors (~2-3 μm in diameter) are located within the dermal layer of the skin. They are activated following the displacement of hair[29, 30] and motion moving across the skin.[30]

Merkel cells and Ruffini endings are slowly adapting, meaning they are active during constant touch or pressure. Merkel cells (~50-100 nm in diameter) are located in the deep layer of the epidermis. They are activated when there is a sustained small indentation in the skin.[30] Ruffini endings are located in the subcutaneous tissue layer of the skin and joints (details regarding their joint functions will be discussed in the next section). They are activated when a sustained stretch is placed on the skin[29] or during touch, pressure, and vibration.[31]

Muscle and Joint Proprioceptors. Proprioceptors are receptors responsible for detecting movement, mechanical stresses, and position.[28] They include muscle spindles, Golgi tendon organs, Ruffini endings, Pacinian corpuscles, and Golgi tendon organ-like endings.

Muscle spindles are intrafusal fibers enclosed in a connective tissue capsule.[29, 32] Two types of intrafusal fibers, which differ in function, are the nuclear bag and nuclear chain fibers. Nuclear bag fibers (~17 μm in diameter) are clustered together in a group.[32] They contain the Group I afferent (aka Ia afferent or primary afferent) neural fibers that spiral around the equatorial region of the muscle spindle. Two subtypes of the nuclear bag fibers are dynamic bag fibers and the static bag fibers. Dynamic bag fibers are sensitive to the rate of change (velocity) in muscle length. Static bag fibers are sensitive to changes in muscle length.[30]

Nuclear chain fibers (~8 μm in diameter) are about half the size of the nuclear bag fibers and are arranged end to end like the links in a chain. They, like the nuclear bag fibers, also contain primary afferent neural fibers that spiral around the equatorial region

of the muscle spindle. They also, however, contain the Group II (type II afferent) nerve fibers.[32, 33] The nuclear chain fibers are sensitive to changes in muscle position.[32]

Golgi tendon organs (GTOs; ~13-17 μm in diameter) are encapsulated sensory receptors intertwined with a small number of muscle fibers.[33] Each GTO is located in collagen fibers of muscle tendons (musculotendonous junction). During passive or active stretching, GTOs are squeezed by surrounding collagen strands. This squeezing results in the activation and propagation of an action potential to the spinal cord.[32]

Ruffini endings (~5-9 μm in diameter) are a cluster of two to six thickly encapsulated, globular corpuscles with a single mylinated axon. They are located in the skin overlying the knee, the knee joint capsule,[34] cruciate ligaments,[35] collateral ligaments,[36] and menisci.[37] Activation of the Ruffini endings occurs when joint angles change, an appendage moves, during joint rotation,[32] and when there is a change in intra-articular pressure.[11, 38]

Pacinian corpuscles (~8-12 μm in diameter) are thick encapsulated receptors that rapidly adapt to low threshold mechanical stress. They are located in the knee joint capsule, cruciate ligaments,[35] collateral ligaments,[36] fat pads, and medial meniscus.[37, 39] Activation occurs during joint rotation and during joint acceleration or deceleration.[32, 38]

The Golgi tendon organ-like endings (~13-17 μm in diameter) are thinly encapsulated, fusiform corpuscles. They are located in the collateral ligaments[36], cruciate ligaments[34, 40], and medial menisci.[37] Their function is similar to Golgi tendon organs in that they monitor tension, except that the Golgi tendon organ-like endings monitor tension in ligaments at the end range of motion not tendons.[29]

Pain and Temperature Receptors. Free nerve endings (0.5-5 μm in diameter) are receptors activated by the release of noxious chemicals or temperature change (Figure 1). Following tissue trauma, prostaglandin, bradykinin, and potassium are released from the damaged tissue. They bind to free nerve endings and stimulate the release of substance P and calcitonin gene related peptide (CGRP; Figure 1). The release of substance P serves two functions: it binds to mast cells in the vicinity of the injury causing the release of histamine (activates nociceptors in the vicinity of the injury) and causes blood to be extravated from the blood vessels. Calcitonin gene related peptide dilates blood vessels in the vicinity of the damaged area. Its action in conjunction with substance P causes edema formation around the injured area.[31, 41]

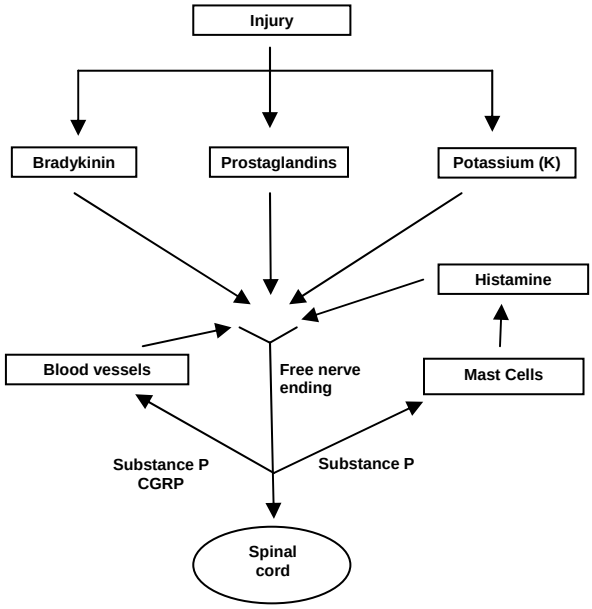


Figure 1. Noxious biological chemicals and their physiological influence on free nerve endings. Adopted from Kandel et al.[41]

Temperature change activates free nerve endings when an object above or below skin temperature is applied to the body. These free nerve endings convey sensory afferent action potentials to the spinal cord.[29]

Neural Innervation of the Knee Articular Structures

The posterior articular nerve (PAN), medial articular nerve (MAN), and lateral articular nerve (LAN) are mixed (sensory and motor) nerves that branch off of the posterior tibial nerve, obturator nerve, and common peroneal nerve, respectively.[38] The posterior articular nerve is the largest nerve supplying the knee joint. It innervates the posterior knee joint capsule, infrapatellar fat pad,[42] oblique ligament, collateral ligaments, cruciate ligaments, and annular ligament.[38] The medial articular nerve branches off the obturator nerve and innervates part of the knee joint capsule, medial collateral ligament, medial meniscus, patellar ligament, and infrapatellar fat pad. The lateral articular nerve branches from the common peroneal nerve and innerves the inferiolateral joint capsule and the lateral collateral ligament.[38]

Spinal Cord

The spinal cord is located in the vertebral foramen of the vertebrae. It receives sensory afferent action potentials from touch, pressure, muscle, joint, and temperature receptors and contains ascending tracts, descending tracts, and spinal interneurons.[41]

The spinal cord is made up of gray matter and white matter (Figure 2).

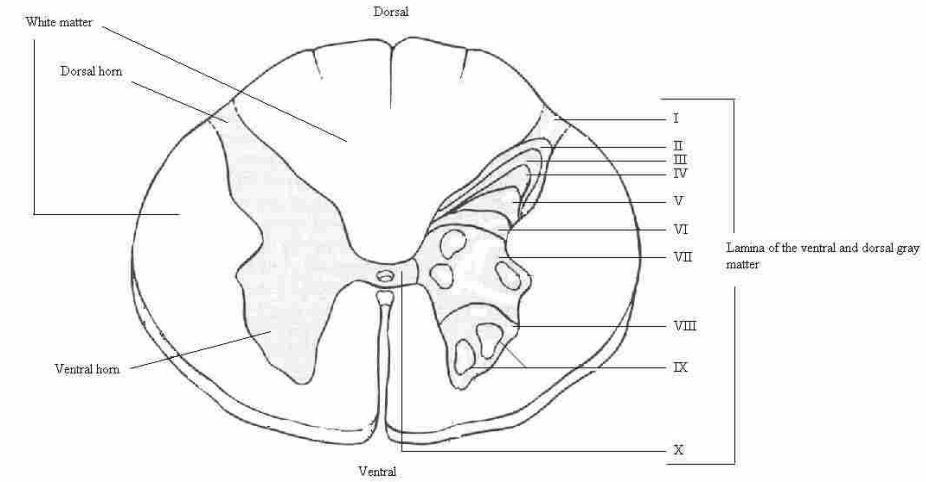


Figure 2. Schematic illustration of the spinal lamina. The left side represents the ventral horn, dorsal horn, and white matter. The right side of the diagram represents the lamina located in the ventral and dorsal horns. A description of these lamina are located in Table 1. Adopted from Martin[43]

The gray matter is divided into bilateral dorsal and ventral horns. The dorsal horns contain sensory neurons that receive input from the periphery and interneurons. The ventral horns contain motor neurons that innervate skeletal muscles and interneurons. The dorsal and ventral horns are divided into lamina (Figure 2 and Table 1). Lamina make up the architecture of the gray matter. The white matter is broken down into the dorsal funiculus (column), lateral funiculus (column), and the ventral funiculus (column). Located within each of these columns are ascending and descending neurological tracts.[44]

Table 1. Lamina Divisions Located in the Ventral and Dorsal Horn of the Gray Matter[43]

Lamina	Location and Function
I	Located in the superficial part of the dorsal horn. It processes nociceptive information. Action potentials conveyed here travel along the A-delta and C-fibers. Also known as the marginal zone.
II	Located ventral to lamina I. Neurons here are almost exclusively interneurons, thus it is involved with interlaminar communication with lamina III and IV. Action potentials conveyed here ascended along C-fibers with some A-delta fibers too. Known as the substantia gelatinosa of Rolando.
III & IV	Located ventral to lamina II. Contain neurons that receive monosynaptic input from A-beta fibers. Involved with interlaminar communication with lamina II.
V	Forms the neck between the ventral and dorsal horn. Action potentials conveyed here ascend along A-beta, A-delta, and C-fibers. Interneurons here synapse with neural tracts that ascend to the brainstem and thalamus.
VI	Forms the base of the anterior horn. Receives action potentials from Ia and Ib afferent neurons.
VII	Makes up most of the intermediate region of the gray matter and extends into the anterior horn. Most Ia afferent neurons synapse here. The lateral part is involved with posture and movement. Interneurons here synapse with neutral tracts that ascend to the midbrain and cerebellum.
VIII	Location varies depending on spinal level. For example, in the cervical and lumbar spine it is in the medial part of the ventral horn. In the thoracic spine it is located in the base of the ventral horn. Projects to other lamina such as lamina VIII on the contralateral side of the spinal cord.
IX	Located in the anterior horn of the spinal cord. Contains the medial, lateral, and central nuclear group of motoneurons each of which contain alpha- and gamma-motoneurons clustered into pools that innervate specific muscles. The medial group innervates axial muscles. The lateral group innervates extremity muscles. The central group innervates the diaphragm and neck muscles.
X	Forms the commissural area between the two halves of the gray matter and surrounds the central spinal canal. Contains neurons and interneurons that cross to the contralateral side of the spinal cord. Receives action potentials from A-delta and C-fibers from the viscera.

Ascending Neurological Tracts

Touch, Pressure, and Proprioceptive Tracts. Action potentials from touch receptors, pressure receptors, and muscle and joint proprioceptors are conveyed to the spinal cord via the A-beta, type Ia afferent, type II afferent, and Ib afferent neurons. These neurons enter the spinal cord via the dorsal horn and synapse with either the

fasciculus gracilis or fasciculus cuneatus. The fasciculus gracilis is located in the central posterior portion of the spinal cord. The neurons that synapse here originate in receptors located in the lower extremity. The fasciculus cuneatus is also located in the posterior aspect of the spinal cord, just lateral to the fasciculus gracilis. The neurons that synapse here originate in receptors located in the upper extremity.[41, 44] Action potentials that synapse with the fasciculus gracilis and fasciculus cuneatus ascend through the spinal cord via the dorsal column to the nucleus gracilis and nucleus cuneatus (nuclei located in the medulla oblongata), respectively. From the nucleus gracilis and cuneatus the medial lemniscus projects these sensory action potentials to the contralateral side of the medulla oblongata before synapsing in the ventral posteriolateral (VPL) nucleus of the thalamus.[41] Action potentials that synapse in the VPL nucleus ascend along thalmocortical fibers to the primary somatosensory cortex and the somatosensory association areas.

Afferent Pain Tracts. Pain action potentials are conveyed to the spinal cord along A-delta and C-fibers. The A-delta fibers are thin, myelinated fibers[29, 41] that convey acute pinprick sensations.[41] The C-fibers are unmyelinated fibers[29] that convey slow, achy, dull pain or burning sensations.[45] At the spinal cord, these fibers synapse with ascending spinal tracts located within the anterolateral system. These tracts are the spinothalamic, spinoreticular, spinomesencephalic, and spinohypothalamic tracts.[30, 41]

The spinothalamic tract is traced to the thalamus.[46] It consists of the neospinothalamic and paleospinothalamic tracts (aka spinoreticulothalamic tract). The neospinothalamic tract receives action potentials directly from the A-delta fibers.[44] Its cell bodies originate in the gray matter of lamina I, V, VI, and VII. From these cell

bodies, axons cross into the white matter and ascend on the contralateral side of the pain stimulus. Termination of the neospinothalamic tract is the ventral posteriomedial (VPM) thalamic nucleus.[44] The VPM nucleus relays the action potentials via thalmocortical neurons to various locations in the brain.[44] The neospinothalamic tract is involved with the localization of pain.[30]

The paleospinothalamic tract receives action potentials from the C-fiber free nerve endings. Its cell bodies originate in the gray matter of lamina VII and VIII. From these cell bodies, axons cross to the contralateral side of the spinal cord before ascending and terminating in the periaqueductal gray. From the periaqueductal gray, nerve fibers convey action potentials to the central lateral thalamic nucleus, centromedian-parafascicular nucleus, and posterior thalamic nuclei.[44] Collectively, these nuclei project action potentials to various locations in the brain. The paleospinothalamic tracts are involved in the suffering or emotional component of pain.[30]

Cell bodies for the spinoreticular tract originate in lamina VII and VIII.[44, 46] Axons from these cell bodies ascend through the spinal cord on both the ipsilateral and contralateral sides of the pain stimulus.[30] Those action potentials that ascend on the ipsilateral side of the pain stimulus terminate in the medullary reticular formation. Action potentials that ascend on the contralateral side also have neurons that terminate in the medullary reticular formation but most of the neurons terminate in the pontine reticular formation. It is reported that action potentials conveyed along the spinoreticular tract are involved with the arousal or attention of a pain stimulus.[30]

Cell bodies for the spinomesencephalic tract originate in lamina I and V.[46] Axons from these cell bodies cross into the white matter and ascend on the contralateral side of the pain stimulus. Termination for this tract is the mesencephalic reticular formation, periaqueductal gray, and superior colliculus; all of which are located in the midbrain.[41] It is thought that action potentials conveyed along the spinomesencephalic tract serve different functions depending on where they terminate. For example, action potentials that terminate in the superior colliculus are thought to correspond with turning the head and eyes towards a stimulus,[30] possibly a painful stimulus. On the other hand, action potentials that terminate in the periaqueductal gray are thought to be involved with emotional aspect of descending pain control.[30]

Cell bodies for the spinohypothalamic tract originate in lamina I, V, VII, X. Axons from these cell bodies ascend to the hypothalamus on both sides of the spinal cord.[47] The exact termination of the spinohypothalamic pathway has not been determined, however, mapping studies indicate that the tract passes through the diencephalon, optic chiasm, and hypothalamus. Action potentials conveyed along this tract are responsible for initiating the emotional and autonomic aspect of pain.[30, 44, 47]

Spinocerebellar Tracts. The spinocerebellar tracts convey action potentials that are not consciously perceived. They include the ventral spinocerebellar tracts, dorsal spinocerebellar tracts, and the cuneocerebellar tract. The ventral and dorsal spinocerebellar tracts originate in Clarke's nucleus. Clarke's nucleus is located anterior to the fasciculus gracilis and fasciculus cuneatus inbetween the second lumbar spine and the eighth cervical vertebrae.[44] These tracts are activated when ascending action

potentials are conveyed from the Ia afferent, type II afferent, and Ib afferent fibers or from efferent action potentials descending along the corticospinal and rubrospinal tracts.[44]

The dorsal spinocerebellar tracts ascends on the ipsilateral side of the spinal cord, synapses in the inferior cerebellar peduncle, and terminates in the intermediate zone of the cerebellum.[33] Action potentials that ascend along the dorsal spinocerebellar tracts originate from muscle spindles, golgi tendon organs, touch and pressure receptors all of which are involved with muscle contraction, muscle tendon tension, position and rate of extremity movement, and joint location.[31, 33] The dorsal spinocerebellar tracts may convey action potentials originating in nociceptive receptors.[48]

The ventral spinocerebellar tracts provide a feedback loop with the cerebellum.[31] They ascend on the ipsilateral side of the spinal cord and synapse with deep cerebellar nuclei in the cerebellum. Mossy fibers located in these deep cerebellar nuclei convey action potentials to the cerebellar vermis.[31, 33] The ventral spinocerebellar tracts form a feedback loop with the corticospinal tracts and rubrospinal tracts. As these tracts descend through the spinal cord they synapse with spinal interneurons that in turn, synapse with the ventral spinocerebellar tract.[33]

The cuneocerebellar tract is the upper limb equivalent to the dorsal spinocerebellar tract.[31, 44] It is activated when ascending action potentials are conveyed from the Ia afferent, type II afferent, and Ib afferent fibers synapse on the lateral portion of the nucleus cuneatus.[44] From the nucleus cuneatus action potentials are conveyed to the ipsilateral inferior cerebellar peduncle and then to the cerebellar vermis.[29, 44] Action

potentials conveyed along the cuneocerebellar tract are involved with limb position and movement.[30]

Brain Processing Areas

The Telencephalon, Diencephalon, Mesencephalon, and Rhombencephalon make up the architecture of the brain. Located within each of these brain regions are different identifiable parts, each of which integrate various types of sensory afferent action potentials and are involved in descending efferent action potentials (Table 2).

Table 2. Basic Overview of the Telencephalon, Diencephalon, Mesencephalon, and Rhombencephalon.

Telencephalon	Largest portion of the brain. It consists of the frontal, parietal, temporal occipital lobes, limbic system, basal ganglia, hippocampus, amygdala, and corpus callosum.
Frontal	The frontal lobe is located in the anterior portion of the cerebral hemisphere. It is responsible for controlling impulses, judgment, language, memory, problem solving, sexual behavior, and socialization. It is also involved with planning, coordinating, and controlling voluntary movements.[30, 49]
Parietal	The parietal lobe is located superior to the occipital lobe and posterior to the frontal lobe. It is responsible for processing sensory information from the senses and is involved with visuospatial processing.[30]
Temporal	The temporal lobe is located on the lateral side of the brain. It is responsible for processing auditory speech information (Wernicke's area in left lobe). It is also responsible for comprehension, naming, and verbal memory.[30]
Occipital	The occipital lobe is located in the posterior inferior portion of the cerebral hemisphere. It contains the primary visual cortex and is responsible for orientation, spatial-frequency color, and visual information.[30]
Limbic system	The limbic system lies beneath the corpus callosum. It is important in the regulation of motor activity and emotional behavior.[30]
Basal ganglia	The basal ganglia consists of a number of structures some of which are controversial. Ultimately involved with motor functions.[30, 41, 50]
Hippocampus	The hippocampus is one of the oldest parts of the brain. It is located within the temporal lobes and is important for memory and spatial navigation (knowing where you are in space).[30]

Table 2 Contineued

Amygdala	A collection of neurons including nociceptive neurons located in the medial portion of the temporal lobes. It is important in the regulation of emotion[30] aggression, jealousy, and fear.[47, 51]
Corpus callosum	The corpus callosum is the physical connection between the right and left cerebral hemispheres. It contains neural tracts that convey information from one cerebral hemisphere to the other cerebral hemisphere.[30]
Diencephalon	The diencephalon is located rostral to the midbrain. It consists of the thalamus, hypothalamus, and the epithalamus.[30]
Thalamus	The thalamus is a collection of nuclei. Its function is to relay action potentials to various locations of the brain.[30]
Hypothalamus	The hypothalamus is located directly beneath the thalamus. It serves as a link between the nervous system and the endocrine system. It is responsible for secreting neurohormones and regulates body temperature, hunger, thirst, and circadian rhythm.[30] Nociceptive neurons have not been well studied here, but stimulation of the periaqueductal gray (PAG) involving the posterior hypothalamus have been used to alleviate pain.[47]
Epithalamus	The most dorsal portion of the diencephalon. It contains the pineal gland which has multiple roles including the regulation of mood.[30]
Mesencephalon	Part of the brain stem. It is responsible for connecting the brain to the spinal cord. The regions that make up the midbrain are the pretectum, tectum (superior and inferior colliculus), cerebral peduncles, midbrain tegmentum, substantia nigra, and red nucleus.
Tectum	A region in the dorsal aspect of the midbrain. It consists of the superior colliculus (contains visual receptors) and the inferior colliculus (contains auditory receptors).
Superior colliculus	Receives visual and some auditory action potentials. Is thought to be involved with head movement towards visual and/or auditory stimuli.[43]
Inferior colliculus	Receives and processes auditory action potentials.[43]
Cerebral peduncles	The cerebral peduncles are a region of the midbrain which contains the midbrain tegmentum, crus cerebri, substantia nigra, and the pretectum.
Substantia nigra	Part of the cerebral peduncles. It is made up of two parts, the pars compacta and the pars reticulate. The pars compacta produces dopamine and is associated with movement. The pars reticulate is responsible visual orientation and eye movement.
Red nucleus	Is located within the midbrain and lies just inferior to the substantia nigra. It is red because it has a rich vascular supply. It is a relay nuclei involved with limb movement.
Rhombencephalon	The most posterior portion of the brain. It consists of the pons and medulla oblongata.[30] Others report it does not consist of the cerebellum,[30] whereas some do.[29]

Table 2 Continued

Pons	The pons is located between the midbrain and the medulla oblongata. It relays action potentials from the cerebral cortex, assists in controlling movement, and is involved with the control of sleep and arousal.[30]
Medulla oblongata	Part of the brain that forms the brainstem and is the physical connection between the spinal cord and pons. It is involved with the control of unconscious function such as breathing, circulation, and muscle tone.[30]
Cerebellum	A structure situated at the base of the brain. It is responsible for motor coordination, posture,[30] and pain.[52]

Investigators using positron emission tomography (PET) neuron-imaging or functional magnetic resonance imaging (fMRI) indicate the primary somatosensory cortex, secondary somatosensory cortex, limbic system (including the anterior cingulate cortex), insular cortex, prefrontal cortex, thalamus, and cerebellum are involved with processing noxious stimulation. [41, 45, 47, 53-55]

Primary Somatosensory Cortex. The primary somatosensory cortex (SI) is located within the parietal lobe. It is somatotopicly organized, meaning neurons are arranged in accordance with parts of the body to which they respond.[45] Evidence of its involvement with processing pain is inconclusive.[55, 56] Both Peyron et al.[55] and Bushnell et al.[56] report some investigators indicate the SIs involvement during noxious stimuli and other investigators report no involvement. They did not, however, indicate who these investigators were. One possible reason for these conflicting results may be the interaction of each anatomical location in the SI. The SI receives action potentials from a number of thalamic nuclei. These nuclei include the ventral posterior lateral, ventral posterior medial, ventral posterior inferior, and ventral intermediate nuclei. It is also divided into four (3a, 3b, 1, and 2) areas. Area 3a receives action potentials from peripheral receptors, specifically muscle afferents which travel through the ventral

intermediate nucleus. Area 3b receives approximately 70% of all axons from the ventral posterior lateral and ventral posterior medial nuclei.[45] Areas 1 and 2 receive action potentials involved in the perception of texture and size of objects. These action potentials travel through the ventral posterior lateral, ventral posterior medial, and ventral intermedius nuclei. Area 2 also receives action potentials from muscle afferents while areas 3b and 1 receive action potentials from cutaneous receptors. [45] With the interaction between all areas, the SI may be involved in identifying a painful stimulus or memory of previous painful experiences.[55, 56]

Secondary Somatosensory Cortex. The secondary somatosensory cortex (SII) is located posteriolateral to the SI in the temporal lobe.[45] It receives action potentials from areas 3a, 1, and 2 of the SI and the ventral posterior lateral, ventral posterior medial, and ventral posterior inferior thalamic nuclei.[57] In addition to receiving action potentials from these thalamic nuclei, neurons from the SII project back to these thalamic nuclei and to the limbic system and insular cortex. It is reported that the SII is involved with the perception and location of the pain.[48]

Limbic System. The limbic system lies beneath the corpus callosum. It consists of the hypothalamus, amygdala, cingulate cortex, hippocampus, parahippocampal gyrus, and nucleus accumbens (Table 3).[51, 54]

Table 3. Summary of Limbic System Structures and their Physiological Functions

Limbic System Region	Function/s
Hypothalamus	Table 2
Amygdala	Table 2
Anterior cingulate cortex	Responsible for behavioral and emotional responses to pain[51, 55, 58]
Hippocampus	Table 2
Parahippocampal gyrus	Involved with spatial navigation (knowing where you are in space).[51]
Nucleus accumbens	Area involved with pleasure and addiction, possibly following a noxious stimulus.[51]

Thalamus. The thalamus is a relay station. It conveys sensory afferent action potentials to cerebral cortices and other brain regions. Four thalamic nuclei activated following noxious stimulation are the posterior part of the ventral posteriomedial nucleus (VPM or VMpo), ventral posterior nuclei (VP), medial dorsal nucleus (MD), and intralaminar nuclei.[47, 59]

The VPM relays pain and temperature action potentials from the spinothalamic tracts to the insular tract. The ventral posterior nuclei (VP) are the main thalamic somatosensory nuclei. They relay action potentials originating in the cutaneous mechanoreceptors to areas 3b and 1 of the SI. Dorsal and anterior to the VPM, the ventral posterior superior nucleus (VPS) relays proprioceptive afferent action potentials to areas 3a and 2 of the SI. Below the VPS, the ventroposterior inferior nucleus relays action potentials to the SII and insular cortices. Action potentials ascending to the medial dorsal nucleus projects to the anterior portion of the cingulate cortex.[45]

The intralaminar nuclei consist of the centromedian, central lateral, parafasicular, midline, and reticular.[43] Following noxious, mechanical, and heat stimuli the centromedian and parafascicular regions are activated. It is reported that these cells may be involved with attention and eye movement with additional input coming from the

cerebellum and superior colliculus.[47] Møller[45] reported the central lateral nucleus projects to the anterior region of the cingulate cortex, a region involved with behavior/emotional responses.

Insular Cortex. The insular cortex is located between the temporal lobe and the parietal lobe. It receives direct projections from the posterior region of the VPM and from the SII. It is involved with visceral sensory sensations, emotional responses, and memory of painful stimuli.[47] For example, when a patient perceives a noxious stimuli as being sharp or dull, they automatically respond to the specific type of pain stimulus.[41]

Prefrontal Cortex. Prefrontal cortex is the most anterior region of the brain lying in front of the primary motor area. It consists of the motor circuit (supplementary motor area), oculomotor circuit (frontal eye field), the dorsolateral prefrontal, lateral orbitofrontal, and anterior cingulate (part of the limbic system). Of these 5 regions, the dorsolateral prefrontal, lateral orbitofrontal, and anterior cingulate may be involved with pain. The dorsolateral prefrontal is responsible for executive functions such as behavior responses, remote memories, generating motor programs, and using verbal skills to guide behavior. The lateral orbitofrontal is responsible for behavior mood shifts from one mood to another.[49] The anterior cingulate is responsible for behavior or emotional responses to pain.

Cerebellum

The cerebellum is involved with the timing of motor activities and in rapid, smooth progressive movements. It helps control the intensity of muscle contraction when

a load is placed on the muscle, and is vital in controlling rapid muscular activities such as running, typing, playing the piano, and talking.[33]

Gross Anatomy of the Cerebellum. The cerebellum contains two deep transverse fissures that divide the cerebellum into three lobes and two shallow grooves. These fissures are the primary fissure and the posteriolateral fissure.[43] The primary fissure separates the cerebellum into anterior and posterior cerebellar lobes. The posteriolateral fissure divides the cerebellum from the flocculonodular lobe. The two shallow grooves run superior to inferior and divide the cerebellar cortex into a vermis and two cerebellar hemispheres.[43]

The vermis is an elevated region in the central portion of the cerebellum. It receives afferent action potentials from visual, auditory, and vestibular regions of the cerebral cortex and from the vestibular apparatus. Efferent action potentials conveyed from the vermis descend to regions of the brainstem responsible for controlling proximal limb muscles of the body.[41]

The cerebellum also consists of two cerebral hemispheres. Each cerebral hemisphere is divided into three divisions. These divisions are the vestibulocerebellum, spinocerebellum, and cerebrocerebellum. The vestibulocerebellum consists of the flocculonodular lobe and portions of the vermis.[33] It receives action potentials from the vestibular (semicircular canals and otolith organs) and visual systems. Action potentials conveyed from the vestibulocerebellum synapse with the lateral and medial vestibular nuclei.[41] The lateral vestibular nuclei assist in controlling the axial and limb muscles

during balance, stance, and gait. The medial vestibular nuclei assist in controlling eye movements and coordinating movements of the head and eyes.

The spinocerebellum makes up most of the vermis and intermediate region of the hemispheres.[32, 33] Action potentials conveyed to the spinocerebellum are initiated by proprioceptors located in skeletal muscles, ligaments, and the joint capsule.[41] They are responsible for coordinating movements of the distal portions of the limbs especially the hands and fingers.[33]

The cerebrocerebellum makes up the lateral hemispheres of the cerebellum. It receives virtually all ascending action potentials from the primary motor cortex, premotor cortex, and somatosensory cortex.[33] Action potentials from the cerebrocerebellum are conveyed through the superior cerebellar peduncle synapsing in the contralateral ventrolateral thalamus and contralateral red nucleus. Axons that synapse in the ventrolateral thalamus continue back to the premotor and primary motor areas, whereas, axons that synapse in the red nucleus form a feedback loop with the lateral hemispheres. It is thought that the cerebrocerebellum is involved with planning complex motor actions, mental rehearsal of movements, and motor learning.[41]

Cytoarchitecture of the Cerebellar Cortex. The cerebellar cortex consists of the Granular, Purkinje, and Molecular layers (Figure 3). The Granular layer is the innermost layer and consists of two interneurons. These interneurons are the Granule cells and the Golgi cells. Granule cells (aka parallel fibers) are tiny neurons approximately 10 μm in diameter. These fibers, which account for half of the neurons in the central nervous

system, project through the Purkinje layer to the Molecular layer, where they synapse with Golgi cell and Purkinje cell neurons.

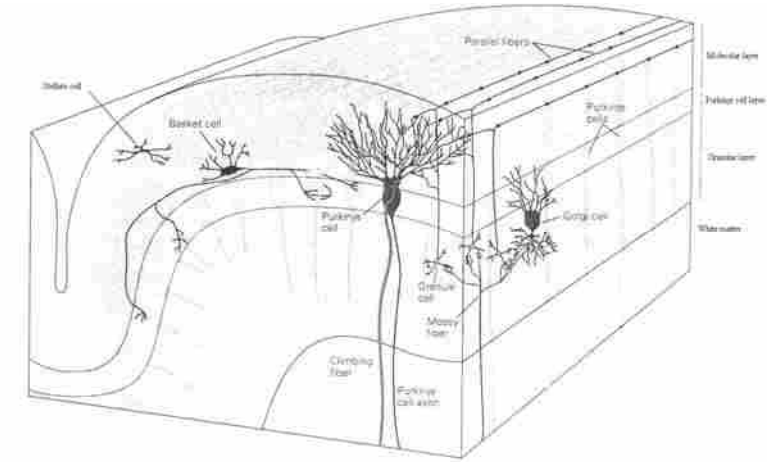


Figure 3. Schematic illustration of the cytoarchitecture of the cerebellum. Adopted from Kandel et al.[41]

The Purkinje layer contains large (50-80 μm) Purkinje cells. These cells contain a large number of axons that extend into the Molecular layer.[41, 60] These axons which are arranged perpendicular to parallel fibers runs through the Purkinje cells, thus each Purkinje cell receives action potentials from the parallel fibers.

The Molecular layer is the outermost layer. It contains two types of inhibitory interneurons (stellate and basket cells) and an excitatory interneuron (granular cells). Stellate cells are located in the out regions of the molecular layer and basket cells are located superior to Purkinje layer. Collectively the stellate cells and basket cells convey inhibitory action potentials to the Purkinje cells.[30, 60]

Cerebellar Afferent and Efferent Neurons. The cerebellar cortex receives afferent action potentials from climbing fibers and mossy fibers.[30] Climbing fibers originate in the inferior olivary nucleus (nuclei in Medulla Oblongata) and wrap around the cell bodies of Purkinje cells.[41, 43] Action potentials conveyed along climbing fibers provide excitatory input to the cerebellum regarding somatosensory information.[41] Mossy fibers originate in nuclei from the spinal cord and brainstem and terminate in the granule cells of the granular layer. Action potentials conveyed by mossy fibers include sensory information from the periphery an well as information from the cerebral cortex.[41]

Purkinje neurons, which are located in the Purkinje layer, are the efferent output of the cerebellar cortex. They synapse on climbing fibers and via an interneuron terminate with mossy fibers. Purkinje neurons also synapse with cells located in the deep cerebellar nuclei (i.e. dentate, interposed and fastigial nuclei) and vestibular nuclei.[60] From these nuclei, efferent projections are sent to the various locations in the brain. For example, neurons from the interposed nuclei synapse in the red nucleus. Neurons in the fastigial nuclei terminate in the vestibular nucleus and the pontine and medullary reticular formations.[60]

Cerebellum and Pain. The cerebellar involvement in pain processing was first reported by Ekerot et al. in 1987.[61] They reported that stimulating A-delta and C-fibers activated climbing fibers located in the cerebellum.[62] Others examining human and animal brains using PET and fMRI reported increases in blood volume to the cerebellar vermis and lateral regions of the cerebellum following acute heat pain, muscle pain, and

capsaicin-evoked pain.[47, 52, 55] They infer that this increase in cerebellar activity may be the cerebellums motor planning processes following noxious stimulation.[54]

Vision, Vestibular, and Auditory Systems

Photoreceptors are vision receptors responsible for converting stimuli into action potentials. Following activation, action potentials initiated by these photoreceptors are propagated by the optic nerves to the optic chiasm. The optic chiasm is a region in the middle of the brain where the optic nerves partially cross each other and terminate. From the optic chiasm the optic nerves become the optic tracts (Figure 4).

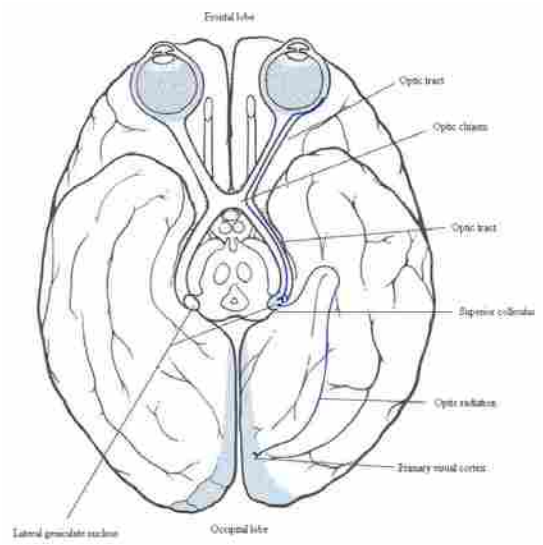


Figure 4. Schematic illustration of the visual pathway.[43]

The optic tracts convey action potentials to three regions of the brain. These regions are the pretectum, the superior colliculus, and the lateral geniculate nucleus. The pretectum is located in the midbrain. It processes action potentials from both eyes regarding the pupillary eye reflex.[41]

The superior colliculus is a paired structure that lies directly beneath the thalamus. It is involved in the generation of saccadic (rapid) eye movements and head-eye coordination. Afferent action potentials conveyed to the superior colliculus also come from the cerebral cortex, inferior colliculus, basal ganglia, and spinal cord.[41] Efferent action potentials conveyed from the superior colliculus project to the paramedian pontine reticular formation and spinal cord. As a whole, the superior colliculus is involved with orienting the head and eyes toward something seen or heard.[33]

The lateral geniculate nucleus receives 90% of the retinal axons; thus it is the primary processing area for all visual information.[41] Action potentials conveyed to the lateral geniculate nucleus travel through 1 of 6 individual layers (1 through 6) of cell bodies before terminating in the primary visual cortex. From these individual layers, action potentials are projected to the primary visual cortex via the Magnocelluar (M) pathway or Parvocellular (P) pathway.[41, 43]

The primary visual cortex (V1) is about 2 mm thick and located in the occipital lobe of the cerebral cortex. It makes up approximately ⅓ of the cerebral cortex and receives action potentials exclusively from the contralateral half of the visual field.[41] It is responsible for motion analysis and color vision.

The visual system also receives vestibular input from the vestibular apparatus. The vestibular apparatus originates in the inner ear, consisting of a bony and membranous labyrinth. The bony labyrinth is a hollow space that contains three semicircular canals (horizontal, anterior, and posterior) and two otolith organs (utricle and saccule).[30] The membranous labyrinth is located within the bony labyrinth and contains a motion sensing

fluid called endolymph. Each semicircular canal is a hollow ring arranged perpendicular to each other. The horizontal semicircular canals communicate at both ends with the utricle, a large dilation of the membranous labyrinth. The anterior and posterior semicircular canals communicate with the utricle at one end, and join each other at the other end.[29]

At the end of each semicircular canal, there is an ampulla. The ampulla is a dilation that contains ciliated sensory hair cells embedded in a gelatinous material called cupula. These ciliated sensory hair cells contain vesicles that store the neurotransmitter. When the neurotransmitter is released from the sensory hair cells, an action potential is conveyed along the vestibulocochlear nerve to the vestibular nuclei.[29]

The vestibular system is constantly active. During any head movement, (i.e. flexion, extension, rotation, elevation, acceleration, or deceleration) endolymph moves from the membranous labyrinth into the ampulla. This movement results in a conformational change in the cupula and hair cells, resulting in the generation and propagation of an action potential. This action potential travels along the vestibulocochlear nerve to the brainstem. Located at the brainstem are four vestibular nuclei (lateral, medial, inferior, and superior), six neural pathways (medial longitudinal fasciculus, medial and lateral vestibulospinal, vestibulocerebellar, the vestibulothalamocortical, and the vesitibuloautonomic).[29]

The lateral and inferior vestibular nuclei convey action potentials down the lateral vestibulospinal tract, through the brainstem, and down the entire length of the spinal cord.

As described earlier, it synapses with interneurons, and alpha- and gamma-motoneurons in lamina VII and VIII.

The superior and medial vestibulospinal nuclei give rise to the medial vestibulospinal tract. It descends bilaterally within the medial longitudinal fasciculus (MLF) and synapses on interneurons, and alpha- and gamma-motoneurons in lamina VII and VIII of the cervical and upper thoracic spinal cord. This tract is responsible for stabilizing head position and maintaining head posture in relation to eye movements.

The MLF and vestibulocerebellar pathways are similar in function. The MLF synapses with the oculomotor, trochlear, and vestibulocochlear nerves and terminates in the oculomotor nuclei. It is responsible for stabilizing visual images when the head moves during walking or running (gaze stabilization). The vestibulocerebellar pathway projects from the vestibular nuclei to the cerebellar hemisphere via the inferior cerebellar peduncle. Axons from the vestibulocerebellar pathway project through the MLF and to the oculomotor, trochlear, and vestibulocochlear nerves to control eye movements and head movement.

The vestibulothalamocortical pathway projects from vestibular nuclei to the thalamus and then terminates in the cerebral cortex. It is responsible for conscious awareness of head position and movement. The last pathway is the vestibuloautonomic pathway. This pathway is beyond the scope of this review; however, it has influence on nausea and vomiting.

The auditory system is anatomically divided into three regions. These regions are the outer ear, the middle ear, and the inner ear.[30, 41] The outer ear consists of the pinna[30] or auricle[41, 43] and external auditory meatus. The pinna captures sound waves and channels them through the external auditory meatus to the tympanic membrane. The middle ear or tympanic cavity is an air-filled space extending from the tympanic membrane to the Eustachian tube.[41]

Also located in the inner ear are three ear bones. These bones, which collectively make up the ossicles are the malleus (hammer), incus (anvil), and stapes (stirrup).[30] The inner ear or cochlea is a snail-shaped organ. Located within the cochlea are three coiled channels. These channels, which contain a fluid called perilymph and extend the length of the cochlea are called the scala vestibuli, scala media, and the scala tympani.

The scala vestibuli is the uppermost of the three channels. It is separated from the scala media by the Reissner's membrane and extends to the oval window where it joins the scala tympani. The scala tympani is the lowermost channel. It is separated from the scala media by the basilar membrane and extends from the round window to the scala vestibuli. The scala media (aka cochlear duct) is located in-between the scala vestibuli, the scala tympani, and is separated by the basilar membrane and Reissner's membrane.[30, 41] Located within the scala media is the organ of Corti (aka organ of hearing).[29] The organ of Corti rests on the basilar membrane. It is composed of two types of hair cell receptors (inner and outer hair cells) and terminal nerve branches from the cochlear nerve.[29]

When sound is conveyed along the external auditory meatus, it vibrates the tympanic membrane and the ossicle bones. Vibrations of the ossicle bones travel through the oval window to the scala vestibuli. At the scala vestibuli a fluid called perilymph is pushed into the scala tympani and to the scala media. As this perilymph is pushed through these channels it causes the basilar membrane which contains hair cells to rub against the tectorial membrane (membrane directly above the basilar membrane) causing friction. This friction results in the bending of hair cells.[43] Bending the hair cells activates the hair cell receptors and stimulates the propagation of an action potential down the cochlear nerve. As this action potential travels down the cochlear nerve it synapses in three regions of the brainstem. These regions are the cochlear nuclei, the superior olivary complex, and the inferior colliculus.

The cochlear nuclei are located in the medulla oblongata. These nuclei consist of the anteroventral, posteroventral, and dorsal cochlear nuclei. They are located in the medulla oblongata.[29] The superior olivary complex is located in the pons. It is made up of the medial superior olivary nucleus and the lateral superior olivary nucleus. Neurons in the medial superior olivary nucleus are sensitive to interaural time differences (lag time from when one ear detects sound and the other ear detects the same sound) and to low-frequency tones. The superior olivary nucleus is sensitive to interaural intensity differences (intensity of sound arriving in both ears) and to high-frequency tones.[43]

The dorsal cochlear nucleus projects to the inferior colliculus. The inferior colliculus is located just beneath the superior colliculus. It is the site where virtually all ascending auditory pathways terminate. The inferior colliculus contains two nuclei and a

dorsal cortex. The two nuclei are the central and external nuclei. The central nucleus is the principle site of termination for the lateral lemniscus. The lateral lemniscus is the ascending brainstem auditory pathway. It conveys action potentials from the contralateral dorsal and posteroventral cochlear nuclei and from the medial and lateral superior olivary nuclei to the inferior colliculus. The inferior colliculus also has axons that synapse in the thalamus and continue to terminate in the primary auditory cortex.

The external nuclei are not well understood, through the use of animal research; however, it is suggested that the external nuclei are involved with acousticomotor function, such as orienting the head and body to an auditory stimulus. The function of the dorsal cortex is not known.[43]

The medial geniculate nucleus is another region that receives and processes auditory information. The medial geniculate nucleus is located between the thalamus and the lateral geniculate nucleus. It is divided into 3 division: anterior, posterior, and medial. The anterior division receives afferent action potentials from the central nucleus of the inferior colliculus and projects to the primary auditory cortex. The posterior division receives action potentials from the inferior colliculus and projects to the secondary auditory cortex. Action potentials conveyed along this division are involved with habituation to an auditory stimulus. The medial division receives afferent action potentials from the external nucleus of the inferior colliculus and conveys to the auditory association areas. This medial division also projects to the temporal and parietal association areas and to regions of the basal ganglia. These regions include the

amygdala, putman, and globus pallidus.[30] With these projections to the basal ganglia the medial division may be involved with the emotional aspect of hearing.[30]

The exact mechanism of how the visual, vestibular, and auditory systems influence pain is not known. It is possible that since the superior colliculus (processes visual information) is connected with the cerebral cortex, reticular formation, and spinal cord, it may be involved with orienting the head and eyes towards a pain stimulus or memory of previous painful experiences. In addition, the inferior colliculus (processes auditory information) is connected with the superior colliculus and thalamus. Therefore, it may also be involved with auditory orientation and head or eye movement towards a pain stimulus.

Descending Motoneurons

There are two types of descending motoneurons, upper motoneurons and lower motoneurons. The upper motoneurons originate in various locations in the brain and brain stem and project towards interneurons and lower motoneurons located in the spinal cord. The lower motoneurons are located within the spinal cord and convey action potentials to skeletal muscles.[29]

Upper Motoneurons. The upper motoneurons are classified into activation systems. These activation systems are the medial activation system and the lateral activation system.[29]

Medial Activation System. The medial activation system consists of four descending neural tracts, all of which originate in the brainstem or the cerebral cortex. These tracts include the tectospinal, medial reticulospinal, medial vestibulospinal, lateral

vestibulospinal, and medial corticospinal (originates in the cerebral cortex). The tectospinal tract originates in the superior colliculus and crosses to the contralateral side of the spinal cord before descending through the brainstem and terminating with lower motoneurons in lamina VI through VIII (See Table 1 and Figure 2) of the first four cervical vertebra. Action potentials conveyed along the tectospinal tract are involved with orienting an individual towards a visual and/or auditory stimulus. This stimulus causes a reflexive turning of the head towards that stimulus. Action potentials that travel along the tectospinal tract also synapse in regions of the vestibular nucleus involved with head and eye movements used in tracking a moving object.[60]

The medial reticulospinal tract originates in the pontine nuclei of the reticular formation. It descends through the spinal cord ipsilaterally and synapses with the lower motoneurons. Action potentials that synapse on these lower motoneurons activate the extensor muscles of the lower extremity.

The medial vestibulospinal tract originates in the medial vestibular nuclei in the medulla oblongata. It descends bilaterally through the spinal cord and terminates in the cervical and upper thoracic spinal cord. Action potentials conveyed along the medial vestibulospinal tract are responsible for activating muscles in the neck.

The lateral vestibulospinal tract originates in the lateral vestibular nuclei of the medulla oblongata. It descends ipsilaterally through the anterior portion of the brainstem, cervical, thoracic, and lumbosacral regions of the spinal cord, and terminates in the medial portions of lamina VII and VIII. This tract is responsible for activating motoneurons supplying extensor muscles of the neck, back, and the limbs. It is also

responsible for inhibiting lower motoneurons (via the Ia inhibitory interneuron) supplying the limb flexor muscles. Its function is to maintain balance and posture while standing or during walking.[29]

The medial corticospinal tract originates in the cerebral cortex. It descends through the anterior brainstem and extends into the thoracic spinal cord. It is responsible for controlling neck, shoulder, and trunk muscle movements.[29]

Lateral Activation System. The lateral activation system consists of the lateral corticospinal tract, rubrospinal tract, and the lateral reticulospinal tract. The lateral corticospinal tract originates in the primary motor cortex. It descends through the anterior portion of the midbrain, crosses to the contralateral side in the medulla oblongata and synapses with interneurons and lower motoneurons.[60] An important function of this tract are its branches that synapse with lower motoneurons controlling the hand and finger muscles.[60]

The rubrospinal tract originates in the red nucleus of the midbrain.[29, 30, 60] It descends through the brainstem and spinal cord, running parallel with the lateral corticospinal tract and synapses with lower motoneurons in lamina V, VI, and VII.[30] The functional role of the rubrospinal tract in humans is unclear,[60] however, investigators examining primates have indicated that the tract plays a role in controlling the upper extremity limb muscles.[29]

The lateral (medullary) reticulospinal tract originates in the pontine nuclei of the reticular formation. It descends bilaterally through the spinal cord and terminates in lamina VII and VIII.[30] It is reported that this tract has very few synapses with alpha-

motoneurons. Instead, the tract primarily synapses on the gamma-motoneurons. Its function is the maintenance of posture[30] where flexor and extensor muscles are facilitated or inhibited during movement.[29, 30] For example, during walking the lateral reticulospinal tract may activate the agonist muscles and inhibit the antagonistic muscles.[29]

Lower Motoneurons. Lower motoneurons are located in four regions of the spinal cord. These regions, which are anatomically arranged, include the posterior, anterior, medial, and lateral regions.[30] The posterior region consists of motoneurons that innervate the flexor muscles. The anterior region contains motoneurons that innervate the extensor muscles. The medial region contains motoneurons that innervate the proximal limb muscles. The lateral region contains motoneurons that innervate the distal muscles.[30]

Located within these four regions, are the alpha-motoneurons and the gamma-motoneurons. Alpha motoneurons (~14 μm in diameter)[33] are heavily myelinated descending lower motoneurons. They originate in the anterior horn of the spinal cord, exit through the anterior roots, and course distally as peripheral nerves. Each alpha-motoneuron innervates skeletal muscle.[30] Gamma motoneurons (~5 μm in diameter)[33] are medium myelinated descending lower motoneurons.[29] They, like the alpha-motoneurons, originate in the anterior horn of the spinal cord and course distally as peripheral nerves. There are two subtypes of the gamma-motoneurons. These subtypes are the dynamic gamma-motoneurons and the static gamma-motoneurons. The dynamic gamma-motoneurons are associated with the dynamic nuclear bag fibers, whereas the static gamma-motoneurons are associated with the static nuclear bag fibers.

Efferent Pain Tracts

Efferent pain tracts differ between the emotional response to pain and localization of pain. For emotional pain, modulation begins in the frontal lobe and limbic system. Action potentials conveyed from the frontal lobe descend to the periaqueductal gray via the anterior trigeminothalamic tract.[30] From the periaqueductal gray action potentials are conveyed to the raphe nucleus magnus. Within the raphe nucleus magnus, interneurons connect the anterior trigeminothalamic tract to the spinal trigeminal tract and to raphespinal fibers. These raphespinal fibers descend down the spinal cord and pass through lamina III and IV before terminating in lamina II (Figure 5).[30]

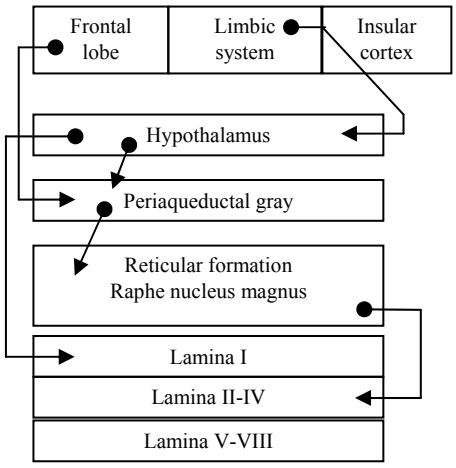


Figure 5. Illustration for descending pathways for emotional pain.[30]

As the raphespinal fibers travel through lamina III and IV they synapse with interneurons. These interneurons project through other laminar regions connecting the A-delta fibers, C-fibers, and the anterolateral tract(Figure 6).[30, 44] Also located within

lamina III, IV, and V are Ia and Ib afferent fibers. These neurons synapse with other interneurons that project to the posteriolateral column.[30, 44]

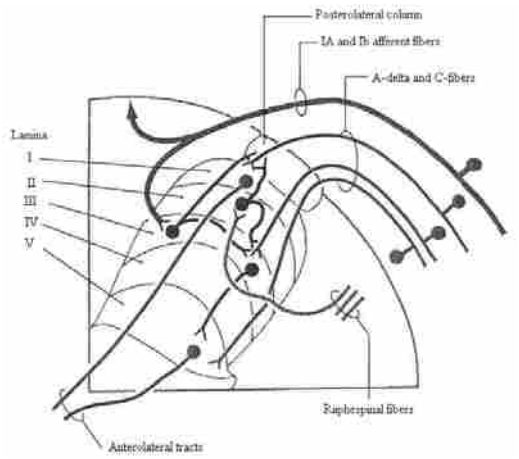


Figure 6. Interneuron convergence between descending and ascending neural fibers and tracts.[30]

Action potentials conveyed from the limbic system descend through the insular cortex to the hypothalamus. From the hypothalamus, neurons project through the periaqueductal gray to the raphe nucleus of the reticular formation. From the raphe nucleus, neurons descend down the spinal cord and synapse on interneurons in lamina II (substantia gelatinosa; Figure 5).[30]

The localization of pain begins in the primary somatosensory and secondary somatosensory cortices. From the primary somatosensory cortex, descending action potentials are conveyed to the thalamus, periaqueductal gray, raphe nucleus magnus, and lamina II-VIII. From the secondary somatosensory cortex, action potentials are conveyed to the thalamus and through the insular cortex before terminating in the periaqueductal gray, raphe nucleus magnus, and lamina II-VIII (Figure 7).

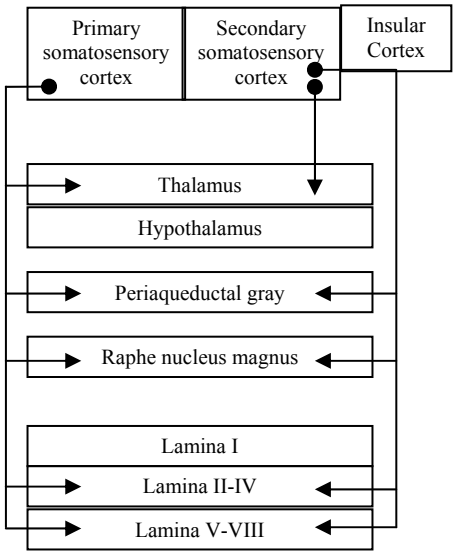


Figure 7. Illustration of descending pathways for the localization of pain.[30]

PAIN

Pain is a protective mechanism for the body.[33] It involves a distinct sensation with complex interactions between sensory, emotional, and behavioral factors.[41] Pain is classified into two types: acute and chronic. Acute pain occurs following a noxious stimulation to the skin such as a pinprick sensation.[45] The pinprick sensation consists of a short-latency and late-burning or emotional involved sensation. The short-latency component produces a distinct sensation that is described as something that "hurts" and is mediated by fast-conducting A-delta fibers.[45] The late-burning and emotionally involved component of pain occurs immediately following the short-latency component and varies in intensity. This type of sensation is mediated by slow conducting C-fibers.[45]

Chronic pain is any type of pain that lasts for an extended period. This type of pain may be caused by continuous stimulation of peripheral nociceptors or changes in

brain function as a result of the long-lasting input from peripheral nociceptors.[45] Table 4 is a summary of the differences between acute and chronic pain.

Table 4. Characteristic Differences between Acute and Chronic Pain[63]

Characteristic	Acute	Chronic
Biological function	Warning	None
Time frame	< 1 month	> 1 month
Fiber transmission	A-delta & C-fibers	C-fibers
Patient localization	Well localized and defined	Poorly localized
Verbal descriptors	Sensory (shooting, hot, sharp)	Emotional (long lasting)
Symptoms & dysfunction	Present, easily identifiable	Absent or can't identify
Physical activity	Diminished with gradual return	Diminished to absent
Social activity	Diminished with gradual return	Diminished to absent

Gender Differences in Pain

Pain between genders is not consistent across studies.[64-67] Some report hormonal changes (menstruation), type of experimental pain stimulus (i.e. electric, thermal, or pressure), environment in which an experiment takes place, gender of the experimenter, presence of other people, subjects attitude towards pain, laboratory setting, anxiety, or expectations of a painful stimulus all contribute to differences between genders.[64, 66]

Although there are inconsistencies within the literature Fillingim and Maixner[66] report that females are more sensitive to pain than males. Females tend to have higher pain levels, a lower threshold to pain, and a lower tolerance of pain than men.[64, 65] One reason why women tend to report differently than men is neural activation and social conditioning. In one study, investigators reported that females exhibited greater activation in their prefrontal cortex than males. The prefrontal cortex is a region of the brain involved with knowledge (memory) and recognition.[68] In regards to social conditioning, it is reported that males are socially conditioned to not express pain for it is a sign of weakness.[66] With inconsistencies between the genders due to the reported

changes in neural activation and social conditioning we are going to focus on male subjects.

Neurotransmitters and Pain

Neurotransmitters are chemicals stored in vesicles located in the postsynaptic membrane. Following an action potential, neurotransmitters are released from these vesicles where they diffuse across a synaptic cleft to bind to specific receptors located on a postsynaptic neuron. In essence neurotransmitters are responsible for relaying electrical signals between neurons and/or organs.[43]

There are many different neurotransmitters located throughout the nervous system each of which is classified into groups. Three common classification groups are: peptides, amino acids, and monoamines. Of these three classification groups, peptides and amino acids are reported to be involved with pain.[50] The peptide neurotransmitters directly involved with pain include substance P, enkephalin, endorphin,[43] dynorphin, and endomorphin.[69]

Substance P is involved with the transmission of pain signals from the periphery to central nervous system. It is reported that approximately 20% of the cells located in the dorsal root ganglion of the spinal cord respond to substance P.[70] Endorphin, enkephalin, dynorphin and endomorphin are endogenous opiates. They function by reducing the perception of pain during stressful conditions.

An amino acid neurotransmitter directly involved with pain is γ-aminobutryc acid (GABA). GABA is a major inhibitory neurotransmitter located in the dorsal horn of the spinal cord[71] and brain.[72] It is responsible for more than 40% of all inhibitory processes.[73]

GABA operates by binding to three types of receptors. These receptors are the $GABA_A$, $GABA_B$, and $GABA_C$. $GABA_A$ receptors are broken down into a number of subsets including the α 1-6, β 1-3, γ 1-3, δ, ε, π, and θ.[74] These receptors which are located in the cerebral cortex, thalamus, hippocampus, cerebellum, amygdala, and substantia nigra are responsible for fast inhibitory transmission.[74] However, other investigators have reported that $GABA_A$ in addition to $GABA_B$ are located on A-delta and C-fibers. For example, in one study,[75] GABA administration caused a significant change in conduction velocity in both the A-delta and C-fiber neurons. Therefore, indicating these receptors involvement in pain.

Identification of $GABA_C$ receptors are fairly new. Their function is similar to the $GABA_A$ receptors; however, they are responsible for slow inhibitory transmission. In addition, $GABA_C$ receptors are located in the brain; however, their greatest concentration is in the retina.[76]

Pain Theories

Theories have evolved from the accumulation of scientific evidence.[77] They give rise to new investigations, which in turn, provide evidence that previous theories may or may not be correct. Considering the complexity of pain physiology, scientists have developed pain theories. These pain theories are the Specificity Theory of Pain, Von Frey's Theory, Pattern Pain Theory, Gate Theory of Pain, Central Biasing Pain Theory, Endogenous-Opiates Pain Theory, and the Neuromatrix Theory of Pain.

Specificity Theory. According to Ignelzi[78] and Melzack[79] the first pain theory, the Specificity Theory of Pain, was introduced by Müller in 1826. In their manuscripts they

indicated that Müller reported specific nociceptors activated and an action potential is conveyed to the brain via the specific neural tracts. [78-80] The action potentials conveyed along these tracts results in the pain stimulus. The idea that specific nociceptors cause pain is a physiological fact; however, the direct connection between a receptor being stimulated and pain is a weakness of this theory. Melzack[79] reported a significant flaw in the specificity theory. Patients with phantom limb pain feel pain, even though they are missing an appendage, or that some human/animals responses can be trained to react favorably to noxious stimuli.

Von Frey's Theory. In 1895 Von Frey extended Müller's theory. He proposed that there are four cutaneous modalities, each of which has one form of energy to which they are sensitive. These four cutaneous modalities are Meissner corpuscles (in addition to hair cells) for touch, Ruffini endings for warmth, Krause end-bulbs for cold, and free nerve-endings for pain. Von Frey assumed that a single receptor lay beneath each sensory spot on the skin and was assigned a definite receptor. This assumption was based on logical deduction rather than experimental evidence. He also postulated that there was a direct line of communication from the skin to the brain which included distinct nerve and pathways of the four different specific receptors in the brain.[81]

Pattern Pain Theory. The Pattern Pain Theory (aka Nonspecific Pain Theory) was introduced by Weddell [82] and Sinclair[83] in 1955. This theory denies that pain receptors exist and suggests that pain occurs when the rate and pattern of sensory input exceeded threshold. According to this theory, all fiber endings are alike, so that the pattern for pain is produced by intense stimulation of nonspecific receptors. These

nonspecific receptors then convey action potentials to the brain where they respond to pain.

The Pattern Pain Theory has a significant flaw. It ignores the fact that there are specialized receptors that respond to chemicals released following injury.[79] This was observed in 1962 when Zotterman reexamined the Pattern pain theory and noted that a brief noxious stimulus such as a pinprick to the skin resulted in two sensations. The first sensation was a fast stinging pain that traveled along the "A" fibers and a slow or burning sensation which traveled along the "C" fibers.[84]

Gate Theory of Pain. The Gate Theory of Pain was developed by Melzack and Wall in 1965.[85] They reported any stimulus causing pain resulted in the activation of pain receptors. These pain receptors initiate the propagation of action potentials to the spinal cord by fast conducting (15 m/s) A-delta fibers and slow conducting C-fibers (2 m/s). At the spinal cord, these A-delta and C-fibers synapse with transmission (T) cells which modulate a spinal gating mechanism (substantia gelatinosa or lamina II; Table 1).

The spinal gating mechanism is the convergence of large diameter (A-delta) and small diameter (C-fiber) nerve fibers. When the large diameter A-delta fibers synapse in the substantia gelatinosa, the substantia gelatinosa reduces the membrane potential thus resulting in presynaptic inhibition (closing of the gate). Small-diameter C-fibers also stimulate the transmission cells but inhibit the substantia gelatinosa thus turning the existing presynaptic inhibition off (disinhibition). This disinhibition results in keeping the gate open. When the gate is open, action potentials travel to the central brain (cerebral cortex). This region of the brain is responsible for processing painful sensation

and initiating an efferent response. These efferent action potentials conveyed down the spinal cord either activate or inhibit pain action potentials.[85]

The substantia gelatinosa is also influenced by action potentials that descend from the brain. If action potentials facilitate the substantia gelatinosa, substance P is released. Substance P is a potent chemical mediator. When released, it binds to receptors on the postsynaptic membrane of the spinothalamic and/or the spinoreticular tracts resulting in the propagation of an action potential to the reticular formation (midbrain). The reticular formation stimulates an autonomic motor and sensory response resulting in action potentials being conveyed to other structures of the midbrain and cerebral cortex.[85]

The cerebral cortex processes pain and conveys efferent action potentials down the spinal cord in order to produce movement. This movement involves hand shaking or rubbing the painful area. By shaking or rubbing the hand, the A-beta fibers are activated. These A-beta fibers move at a faster rate (70m/s) than the A-delta nerve fibers. Therefore, it reaches the substantia gelatinosa more quickly than another painful stimulus. Action potentials from the A-beta nerve fibers occupy the gate, decreasing the pain impulse to the T cells. This process of decreasing pain will continue as long as the A-beta fibers are activated. However, as the A-beta nerve fibers become inactivated, action potentials from these fibers no longer occupy the gate and action potentials from the A-delta fibers and C-fibers are sent back to the spinal cord and brain.[86]

Central Biasing Pain Theory. The Central Biasing Pain Theory (aka Central-Control-mechanism Theory) explains the concept of a "learned behavior." This theory builds on the Gate Control Theory of Pain and addresses how the brain influences both

incoming and outgoing messages.[86] The central control (brain) stores information related to previous painful experiences. This storage plays a factor in the body's response to future painful experiences. For example, when a patient is unconsciously aware of an injury, their response may be minimal until they become consciously aware. Immediately following conscious awareness the patient reacts to injury. In essence, becoming consciously aware alters the patient's perceived response.[86]

Endogenous-Opiates Pain Theory. According to Aronson,[86] the Endogenous-Opiate Pain Theory was introduced by Castel in the 1979. In describing the theory, Castel reports the body produces three peptides with opioid-like properties: β-endorphins, dynorphins, and methionine enkephalins.[86]

Beta-endrophin is an opiate-like substance, similar to morphine.[87] It is produced in the anterior pituitary gland and neurons in the hypothalamus that project to the periaqueductal gray.[88] When β-Endorphin is released, it circulates via the blood stream and binds to opioid receptors; producing analgesic effects.[87] Dynorphin is released from the periaqueductal gray. It is involved with suppressing the response to noxious stimuli.[88] Methionine enkephalin is released from the spinal cord in response to the release of substance P.[69] It functions by counteracting the effect of substance P by inhibiting transmission cells in the substantia gelatinosa.[69, 88]

Neuromatrix Theory of Pain. The Neuromatrix Theory of Pain was published in 1999 as an extension of the Gate Theory of Pain.[89, 90] In it, Melzack explained the brain's role in understanding pain. He reported that the brain has genetically built-in matrices of neurons (neuromatrix) which are sculpted by sensory input. These matrices produce

characteristic nerve impulse whose spatial distribution and synaptic links are genetically determined. Areas of the brain involved consist of loops between the thalamus and the cerebral cortex (thalamocortical) and between the cerebral cortex and the limbic system.[77] The thalamocortical and limbic loops diverge into various areas in the brain. They allow parallel processing in different components of the neuromatrix and interact with one another. This interaction forms cyclical processing's resulting in the synthesis of nerve impulses, thus forming a "neurosignature".[89-92]

One could say pain is purely a sensory phenomenon, yet injury does not merely produce pain; it disrupts the brain's homeostatic regulation system. Disruption of the homeostatic system by means of physical injury results in a series of physiological events. For example, following physical injury, neural, hormonal, and behavioral activities aimed at returning the body back to homeostasis are activated. The specific physiological programs activated are selected genetically and influenced by the type and severity of the injury.[90] For example, these regulatory systems initiate a sequence of events to reinstate homeostasis. These events involve the release of cytokines such as gamma interferon, interleukins 1 and 6, and tumor necrosis factor into the blood stream.[90] Once in the blood stream, these cytokines travel to the brain and activate receptors responsible for conveying action potentials to various brain regions. In addition to evaluative information from the brain, these cytokines initiate a sequence of activities similar to the acute inflammatory process.

In the event of severe injury, adrenalin is released into the bloodstream and the coeruleus/norepinephrine system in the brainstem is activated. This activation causes

action potentials to be conveyed to various locations in the brain and to descending efferent sympathetic nerve fibers. The results of this activation causes all body organ systems to be recruited in order to restore homeostasis.[90, 91]

Melzack also reports how the Neuromatrix Theory of Pain may describe chronic pain.[90] Painful sensations alter an individual's injury perception causing the release of adrenocorticotropic hormone (ACTH) from the anterior pituitary gland. Adrenocorticotropic hormone travels via the blood stream to the adrenal gland where it stimulates the release of cortisol. Cortisol is a potent hormone that may play a role in determining chronic pain. Cortisol, an essential hormone for survival, is responsible for producing and maintaining high levels of glucose for rapid response after injury, threat, or other emergencies. Cortisol, however, is a destructive hormone. It breaks down skeletal muscle protein and inhibits calcium, thus affecting skeletal bone growth. Elevated/sustained cortisol levels can produce myopathy, weakness, fatigue, and decalcification of bone, thus producing some forms of chronic pain.[90, 91]

Cortisol may also cause chronic pain by having a direct influence on the hippocampus.[90] As individuals age, there is a natural loss of neural fibers in the hippocampus. This loss reduces a natural brake on cortisol release which is normally exerted by the hippocampus. As a result, cortisol is released in larger quantities causing a greater loss of neural fibers located in the hippocampus. This neural collapse has been reported in aging primates and presumably occurs in humans. This neural collapse may explain why there is an increase in chronic pain among older individuals.[90, 91]

The release of cortisol alone may not be sufficient to cause chronic pain. Cortisol release in addition to biological/psychological factors may contribute to chronic pain. These factors, which may act alone or together in the release of cortisol include sex-related hormones, genetic predispositions, stress derived from every day life, or social competition.[90, 91]

The Neuromatrix Theory of Pain proposes that the neurosignature for pain is determined by synapses in the neuromatrix composed of both genetic and sensory influences. The neurosignature pattern is also modulated by sensory information and cognitive events. In short, the neuromatrix is a homeostatic-regulatory system and when the body is under stress the homeostatic system fails causing the release of hormones. These hormones give rise to chronic pain that so far have been resistant to conventional treatments used to minimize pain.[90, 91]

The Neuromatrix Theory of Pain provides a guide away from the sensory perception of pain. It directs us towards evaluating the multidimensional or multiple physiological influences associated with the development of pain. These influences may range from the neuromatrix, which is genetically determined, sensory action potentials, and anatomical systems such as the endocrine or immune systems and from other areas in the brain.[92]

Measuring Pain

Following a noxious stimulus, it is not uncommon for clinicians and scientists to quantify a patient's perceived pain using a pain scale. There are many different pain scales used to quantify pain: including, number rating scale,[93] graphic rating scale, verbal

rating scale,[93] McGill pain questionnaire,[27] short-form McGill pain questionnaire,[94] and visual analogue scale.[93]

Number Rating Scale. The number rating scale (e.g. Borg Scale of Perceived Pain)[95] consist of a series of numbers ranging from 0 to 10 or 0 to 100, with endpoints representing the extremes of pain and labeled "no pain" and "worst possible pain", respectively.[96] Patients choose the number that best corresponds to their level of pain.[95, 96] Prior to a treatment, during a treatment, and following a treatment patients select which number best describes their level of pain.

Graphic Rating Scale. The graphic rating scale (GRS) contains descriptors placed at equal intervals along a scale. Descriptors such as the following have been used to describe pain intensity: no pain, dull ache, slight pain, more slight pain, painful, very painful, and unbearable pain.[26] Although this method of measuring pain has been used clinically and in research, one should look at it with skepticism. For example, these descriptive words may lack sufficient sensitivity to measure pain, whereas, the placement of the descriptors along the base of the pain scale creates an expression of the pain experience or intensity and forces a patient or subject to transform feelings into words.[26]

Verbal Rating Scale. The verbal rating scale consists of a group of word descriptors without numbers.[95] For example, no/mild/moderate/severe/unbearable pain are most widely used.[97] When administered, patients verbally rate their pain as absent, mild, moderate, or severe. The major problem with the verbal rating scale is that it forces a patient to translate their feeling into words, which does not express exactly what a

patient is experiencing. In addition, all words used do not necessarily mean the same thing to each patient.[97]

McGill Pain Questionnaire. The McGill Pain Questionnaire is the most comprehensive and complex pain-measuring instrument. It consists of the following four parts.[95] 1) Patients circle the location of their pain on a pair of images (anterior and posterior view of a human drawing). 2) Patients are given a questionnaire consisting of 20 groupings of 3 to 5 associated words. The 20 groupings are then divided into 4 subclasses, each of which measures one of the qualities of pain: sensory pain (groups 1-10), affective pain (groups 11 to 15), evaluative pain (group 16), and miscellaneous pain (groups 17 to 20).[27] Patients are instructed to choose no more than one word in any group but are not required to choose a word from each group. 3) Patients then choose 3 groups of words which represent consistency of the pain. These words include constant, intermittent, or transient pain. 4) Patients select the strength of their pain. In describing the strength, patients choose 1 of 5 descriptors that best describes the intensity of their pain. These words include mild, discomforting, distressing, horrible, and excruciating.[95]

There are four types of data that can be obtained from the McGill Pain Questionnaire. These are the pain rating index sum (PRI) (S), pain rating index rank (PRI) (R), number of words chosen (NWC), and the present pain intensity (PPI).[27] The (PRI) (S) consists of the sum total for all words chose in a category and for all categories. For the (PRI) (R) words in each grouping are ranked. The words are ranked to implying the least pain is given a value of 1, the next word is given a value of 2 and so on. The values of the words are chosen by the subject and then added up to obtain a score for each

grouping and a total score for all groupings. The NWC simply implies the number of words a subject selects. The PPI is a number-word combination. It is used to determine the overall pain intensity at the time of administering the questionnaire. By using this method of analysis, the questionnaire is administered before and after a procedure or treatment, the difference can then be expressed as a percentage of change from the initial questionnaire.[27] A few investigators have used the McGill Pain Questionnaire to grasp an understanding on the quality of pain.[42] In these investigations, words such as aching, throbbing, spreading, and nagging were selected in one investigation[42]; aching, annoying, throbbing, nagging, and dull were selected in another investigation[98]; and taut, drilling, and tight were selected in a third investigation.[99]

Short-Form McGill Pain Questionnaire. The Short-Form McGill Pain Questionnaire (SF-MPQ) was developed by Melzack for the use of specific research settings when the time to obtain information from a patient is limited.[94] The form consists of 15 representative words from the sensory (n = 11) and affective (n = 4) categories from the McGill Pain Questionnaire. It also includes present pain intensity and a visual analogue scale to indicate the overall pain intensity. Each description is given a rank of intensity (0, none; 1, mild; 2, moderate; and 3, severe).[94]

Visual Analogue Scale. The Visual Analogue Scale (VAS) is a common instrument used in quantifying pain. The VAS consists of a horizontal or vertical line typically 10 cm (100 mm) in length with contrasting descriptors at each polar end.[96, 97] These polar descriptors are typically "no pain" on the left end and "unbearable pain,"[95] "worst pain ever,"[96] "intolerable pain" on the right end. With the VAS there are no

numbers so patients make a mark on the line before and after some form of intervention.[96] The differences between the two marks are then compared. A major advantage of the VAS is its simple tool. Patients can easily understand the instructions and the scoring process is relatively simple.[96] Numerous investigators examining experimental pain induced by hypertonic saline have used the VAS before a treatment, condition, or test and every few seconds to a minute during the treatment, condition, or test.[18, 19, 22-24, 99-106] In these investigations, however, investigators neglect to inform the reader if subjects were able to observe their pain measures as they continue to indicate their level of pain. In one article it was reported that when a VAS is repeated within a short space of time (~ 1 minute), the scores were reliable ($r = .99$).[107]

Experimental Pain

Pain physiology is difficult to study in injured patients because of the variability between patients. Pain models, therefore, have been developed to induce pain in uninjured people. These models of inducing pain include:

- Cold presser test[108-111]
- Electrical stimulation[108, 112, 113]
- Noxious heat application[108, 114]
- Capsaicin[115-126]
- Bradykinin[127-129]
- Prostaglandin E2[130]
- Histamine[131]
- Serotonin[127-129]

- Calcitonin gene-related peptide (CGRP)[132]
- Neurokinin A[132]
- Substance P[132]
- Hypertonic saline[17-20, 22-24, 42, 98, 102, 105, 106, 133-147]

Of the experimental pains, hypertonic saline has gained the most acceptance.[17] Hypertonic saline was first introduced by Kellgren in 1938.[145] He reported hypertonic saline was harmless, repeatable, and produced a fairly consistent response.[145] With hypertonic saline, subjects report pain to be aching, throbbing, and nagging.[42] In addition, pain intensity increases rapidly to maximum pain intensity (peak pain) at approximately 3 minutes and subsided slowly leaving no pain approximately 15 minutes after administration. Since the work of Kellgren, other investigators have used hypertonic saline as an experimental pain model in evaluating pain arising from the:

- Infrapatellar fat pad[42, 98, 133]
- Extensor carpi radialis brevis[140]
- Lumbar longissimus muscle[141]
- Tibialis anterior[18-20, 23, 99, 100, 102, 105, 136]
- Biceps brachii muscle[143]
- Gastrocnemius medial head[100, 102]
- Gastrocnemius lateral head[102]
- Extensor hallucis longus[102]
- Soleus[20, 102, 105]
- Lumbar erector spinae muscles[147]

- Paravertebral muscles of neck and back[144]
- Human masseter muscle[106, 146]
- Posterior temporalis muscle[24, 135]
- Abductor digiti minimi[22]
- Dorsal interosseum[22]
- Interspinous ligament[134]

Hypertonic Saline Administration. There are two procedures for administering hypertonic saline: 1) inject a single quantity of saline or 2) continuously infuse the saline using a syringe pump. The concentration, quantity, time, and site of a hypertonic saline injections differ between investigations (Table 5). For example, Graven-Nielsen and Svensson[100] injected 0.5 ml of 5% hypertonic saline over 20 seconds into the tibialis anterior muscle, whereas, Ciubotariu et al.[102] injected 1.0 ml of 6% hypertonic saline into the tibialis anterior muscle. Unfortunately the rationale for why different concentrations and times of administration are not mentioned.

Infusion rates for hypertonic saline also vary between investigations (Table 6). For example, in one investigation, 0.2, 0.5, and 0.9 ml of hypertonic saline were infused for 40 seconds each with a 140 second delay between infusions.[23] Whereas, in a different investigation 0.5 ml, 2.2 ml, and 4.4 ml of hypertonic saline was infused for 20 seconds, 440 seconds, and 440 seconds, respectively.[100]

Through pilot work, our objective was to develop a constant pain stimulus lasting for 20 minutes. Therefore, we examined two published methods of administration: 1) inject 0.5 ml of 5% hypertonic saline[100, 148] and 2) continuously infuse 0.5 ml for 20

seconds, 2.2 ml for 440 seconds, and 4.4 ml for 440 seconds.[99] Following the injection, subjects were pain free approximately 13 minutes after injection. During the infusion, subjects could not stand the pain at approximately 4 minutes into the infusion. Therefore considering these methods of administration did produce a constant level of pain for 20 minutes, we experimented with a number of different infusion rates and noticed that a 20-minute infusion rate consisting of an on/off 3-minute cycle with the last 2 minutes "on" caused patients to perceive a fairly constant level of pain for 20 minutes. In addition an infusion rate consisting of an on/off 3-minute cycle with the last 1 minute "on" caused patients to perceive a fairly constant level of pain for 25 minutes.

Table 5. Summary of Investigators Administering Hypertonic Saline with a Single Injection

Author, Year	Concentration	Quantity/time	Site	Subjects	Results
Feinstein et al., 1954[144]	6% saline	0.5 to 1.0 ml	Each intervertebral space b/w atlanto-occipital & sacrum	5 (no demo)	Local pain at all spinal levels No referred pain radial aspect of the upper limbs and feet
Hockaday & Whitty, 1967[134]	6% saline	0.1 to 0.3 ml	Interspinous ligament	22 males 6 females	Constant and consistent pain at all spinal cord levels
Graven-Nielsen et al., 1997[100]	5% saline 0.9% saline	0.5 ml in 20 s	Exp 1: tibialis anterior Exp 2: medial head gastrocnemius Exp 3: both muscles	Exp 1: 9 males Exp 2: 19 males Exp 3: 10 males	Peak pain ↑ for hypertonic saline Torque ↓ post hypertonic saline not isotonic Muscle pain ↓ endurance time during submaximal contractions
Türp et al., 2002[146]	5% saline	0.2 ml in 15 s	Masseter	10 males 10 females	↓ EMG activity bilaterally post injection in the ipsilateral masseter
Bennell et al., 2004[42]	5% saline	0.1-0.5 ml	Medial infrapatellar fat pad	2 males 9 females	Peak pain 5.8 (NRS) ~ 3 min post injection Pain-free ~15 post injection Knee pain similar to patients with anterior knee pain
Ciubotariu et al., 2004[102]	6% saline	1.0 ml	Tibialis anterior Gastrocnemius	6 males 4 females	↓ endurance time for dorsiflexion & plantarflexion at 50 & 80% MVC ↓ muscle activation in the painful muscles
Bennell et al., 2005[98]	5% saline	0.2-0.25 ml in 10 s	Medial infrapatellar fat pad	5 males 11 females	JPS not affected
Bennell et al., 2005[133]	5% saline	0.2-0.25 ml in 10 s	Medial infrapatellar fat pad	6 males 6 females	Standing balance not affected
Smith et al, 2005[141]	5-7% saline	1.5 ml	Lumbar longissimus	8 males 4 females	↓ lumbar spine movement post hypertonic saline No change in center of pressure
Ervilha et al., 2005[149]	5.8% saline 0.9% saline	1.5 ml in 10 s	Biceps brachii Triceps brachii Biceps & triceps brachii	7 males	↓ motor unit discharge rate with hypertonic saline Conduction velocity not affected by pain
Falla et al., 2006[148]	5.8% saline	0.5 ml	Splenius capitis Sternocleidomastoid	12 males 6 females	↓ EMG activity in agonist, synergist, & antagonist muscles

Table 6. Summary of Investigators Administering Hypertonic Saline with Infusion

Author, Year	Concentration	Quantity/time	Site	Subjects	Results
Graven-Nielsen et al, 1997[19]	5% saline	0.5 ml for 20 s (90 ml/h), 2.2 ml for 440 s (18 ml/h), & 4.4 ml for 440 s (36 ml/h)	Tibialis anterior	11 males	Local pain > than referred pain Referred pain > between 20-460 s than 460-900 s Referred pain intensity delayed compared to local pain
Svensson et al., 1998[104]	5% saline 0.9% saline	0.2 and 0.5 ml both in 20 s	Masseter (0.2 ml) Tibialis anterior (0.5 ml)	10 males	5% saline caused moderate pain (3.6 ± 1.9 cm) as compared to 0.9% 0.3 ± 0.6 cm) Infusion of 5% saline increased EMG activity as compared to 0.9% Pain lasted up to 600 s after 5% saline
Graven-Nielsen et al., 1998[99]	9% saline 0.9% saline	0.5 ml in 20 s	Anterior tibialis	7 males 15 females	No difference b/w hypertonic saline & isotonic saline May be due to superficial injections of lidocaine
Zedka et al., 1999[147]	5% saline	50, 60, 100, 140, 150, and 200 µl min^{-1} for 12 min.	Erector spinae of lumbar spine	4 males 1 female	↓ voluntary movement Symptoms similar to patients with low back pain
Andersen et al., 2000[105]	5% saline	1.0 ml and 2.0 ml in 40 s	Soleus Tibialis anterior	20 males	Inhibition during soleus infusion with concurrent facilitation of tibialis anterior
Birch et al., 2000[150]	5.8% saline 0.9% saline	0.3 ml	Extensor carpi ulnaris	10 females	No difference between 5.8% and 0.9%
Le Pera et al., 2001[22]	5% saline	0.2 ml in 20 s	Abductor digiti minimi Dorsal interosseum	34 males 11 females	Peak pain ~5.8 cm (VAS) at ~142 s post infusion H-reflex ↓ 2-4 min post infusion
Wang et al., 2001[106]	Not reported	0.2 ml in 20 s & 6ml/h in 440 s, & 9 ml/h in 440 s	Masseter	11 male 1 female	Peak pain ~ 4.9 cm (VAS) No pain 5-10 min post infusion
Matre et al., 2002[20]	6% or 9% saline infused	5 ml in agonist muscle in 10 min 10 ml in agonist & antagonist in 10 min	Exp 1: 6% in anterior tibialis Exp 2: 6% in anterior tibialis & soleus Exp 3: 9% in anterior tibialis	Exp 1: 11 females Exp 2: 12 females Exp 3: 10 females	↑ pain with hypertonic saline (VAS) Pain in tibialis anterior & soleus similar Pain in 2 muscles > than 1 muscle Pain altered movement during infusion into 2 muscles, simultaneously
Farina et al., 2004[23]	5.8% saline	0.2, 0.5, and 0.9 ml in 40 s (18 ml/h) Separated by 140 s	Tibialis anterior	5 males 7 females	Motor unit firing rate ↓ as pain intensity increased

Table 6. Continued

Ervillha et al., 2004[143]	5.8% saline	0.5 or 1.5 ml	Biceps brachii	11 male 4 female	1.5 ml ↑ pain more than 0.5 ml ↓ IEMG of biceps brachii ↓ IEMG of brachioradialis & medial head of triceps brachii
Farina et al., 2005[151]	5.8% saline	0.5 ml in 40 s	Tibialis anterior	7 males 4 females	↑ pain with hypertonic (VAS) ↓ motor unit discharge rate during contractions
Peddireddy et al, 2005[24]	5.8% saline 0.9% saline	0.2 ml in 20 s & 6ml/h in 440 s, & 9 ml/h in 440 s	Posterior temporalis	15 males 15 females	No difference in pain b/w gender (VAS) Isotonic saline none to little pain
Farina et al., 2005[18]	5.8% saline 0.9% saline	0.2, 0.5, & 0.9 ml in 40 s Separated by 140 s	Anterior tibialis	12 males	↑ pain with hypertonic saline (VAS) ↓ muscle activity during voluntary contractions
Thurnberg et al., 2005[152]	5% saline	0.3-0.5 ml for 20 m	Erector spinae	19 males	↑ pain with hypertonic saline (VAS) ↑ cerebral blood flow during early pain. ↓ cerebral blood flow during late pain

Hypertonic Saline and Involuntary Motor Output. Few investigators have reported involuntary motoneuron pool excitability following hypertonic saline administration.[21, 22] Le Pera et al.[22] reported that 0.2 ml of 5% hypertonic saline injected into the abductor digiti minimi and dorsal interossei of the hand did not change H-reflex amplitude. There was however, a reduction in H-reflex amplitude at 2 and 4 minutes after peak pain (110 ± 40 seconds postinjection).

Svensson et al.[21] reported no change in motoneuron excitability when 0.2 ml of 5% hypertonic saline was infused into the contralateral masseter muscle for 20 seconds. One explanation for the differences between Le Pera et al. and Svensson et al. was the baseline measures. Svensson et al. measured H-reflex while subjects were clenching their jaw at a level corresponding to 50% of their baseline measure.[21] By clenching the jaw baseline measures for motoneuron pool availability were not achieved, therefore, one can not make comparisons to resting measurements.

Hypertonic Saline and Voluntary Motor Output. A number of investigators have examined voluntary motor activity after the administration of hypertonic saline.[17-21, 23, 24, 99-102, 104-106, 135, 138, 140, 141, 143, 146-148, 150, 151] For example, hypertonic saline decreases endurance time (length of time an individual can voluntarily contract a muscle),[100] and maximal voluntary strength during static and dynamic muscle contractions.[17]

The exact mechanism how hypertonic saline decreases voluntary motor output is not known, however, it is possible that hypertonic saline causes changes in neural drive to motoneurons. Graven-Nielsen et al. [19] report that hypertonic saline administration may activate inhibitory mechanisms such as spinal inhibitory interneurons. By activating

these interneurons inhibitory neurotransmitters may be released resulting in decreased motor output.

In order to determine if hypertonic saline influences voluntary movement, we inserted a small catheter (27 gauge) into the infrapatellar fat pad and connected it to a 30-inch connection tube filled with hypertonic saline. We then had subjects perform extend their knee and noticed that subjects did not fully extend their knee without bending the catheter or connection tube. We therefore can not perform voluntary movement during the infusion of hypertonic saline.

INHIBITION

A natural regulatory occurrence in the neuromuscular system is inhibition.[8] Different types of inhibition found in the neuromuscular system include presynaptic inhibition, postsynaptic inhibition, reciprocal inhibition, recurrent inhibition, and arthrogenic inhibition. Presynaptic inhibition occurs when there is a decrease amount of neurotransmitter release from synaptic vesicles located in the presynaptic neuron. The basis behind presynaptic inhibition is to decrease the effectiveness of one neuron synapsing on another neuron or a membrane.[153] Postsynaptic inhibition occurs when an inhibitory neurotransmitter such as GABA is released from the synaptic vesicles located in the presynaptic neuron. If the neurotransmitter binds to specific inhibitory receptors, the membrane becomes hyperpolarized (more negative), thus making it more difficult for an action potential to occur.[19] Reciprocal inhibition is caused by Ia inhibitory interneuron activity. Recurrent inhibition is mediated by Renshaw cells. Both reciprocal and recurrent inhibitions are discussed later in the spinal inhibitory interneuron section.

Arthrogenic muscle inhibition (AMI) is an ongoing reflex inhibition of the musculature surrounding a joint. It occurs following artificial knee joint effusion[9, 11] and acute[12] or chronic joint pathology.[13, 14, 154]

It is thought that AMI occurs following the activation of many different receptors. These receptors initiate action potentials which are conveyed along specific nerve fibers to the spinal cord. At the spinal cord, these nerve fibers synapse with inhibitory interneurons, whereas these inhibitory interneurons in turn, synapse with motoneurons located in a motoneuron pool. If this interaction with motoneurons decreases the ability to recruit other motoneurons within the motoneuron pool, a reduction in the amount of force would stem from the motoneuron pool.[8]

Some authors attribute AMI to pain,[155] however others[9, 15, 16] report AMI occurs in the absence of pain. For instance, subjects receiving meniscectomies presented with AMI after pain subsided and following the injection of bupivacaine.[15, 16] These subjects also experienced quadriceps inhibition while pain free at 3 to 4 days and 10 to 15 days following the operation. In a different study, artificial knee-joint effusion with 60 ml of sterile isotonic saline caused AMI in the absence of pain.[156] No independent investigation has examined if pain receptor activation is a contributing factor to AMI.

Spinal Inhibitory Interneurons

It is possible that spinal inhibitory interneurons are involved with AMI. Interneurons which are the most common neurons in the spinal cord,[157] receive action potentials from each other, incoming sensory afferents neurons, descending neural tracts originating in the brain and brainstem, and motoneurons[44, 158] such as those terminating in

agonist, synergistic,[159] or antagonistic muscles.[28] Interneurons are primarily located within one spinal cord segment; however, some have axons with collateral branches that terminate in both ipsilateral and contralateral spinal cord segments.[44] Three spinal inhibitory interneurons are Ia inhibitory interneuron, Ib inhibitory interneuron, and Renshaw cells.[44]

Ia Inhibitory Interneurons. Ia inhibitory interneurons are located between the Ia afferent neuron and the alpha-motoneuron of antagonist muscles (Figure 8). Their responsibility is to inhibit the alpha-motoneuron of the antagonist muscle when the agonist muscle is stretched. The Ia inhibitory interneurons also receives excitatory input from joint afferents, cutaneous afferents, and inhibitory input from the corticospinal, rubrospinal, and the vestibulospinal tracts.[157] Action potentials conveyed from these spinal tracts are important in balancing the excitatory and inhibitory input.[157] Ia inhibitory interneurons also prevent activation of Renshaw cells, thus preventing co-contraction of agonist and antagonistic muscles. This process of preventing co-contraction of agonist and antagonistic muscles is mediated by the Ia inhibitory interneuron and is referred to as reciprocal inhibition.

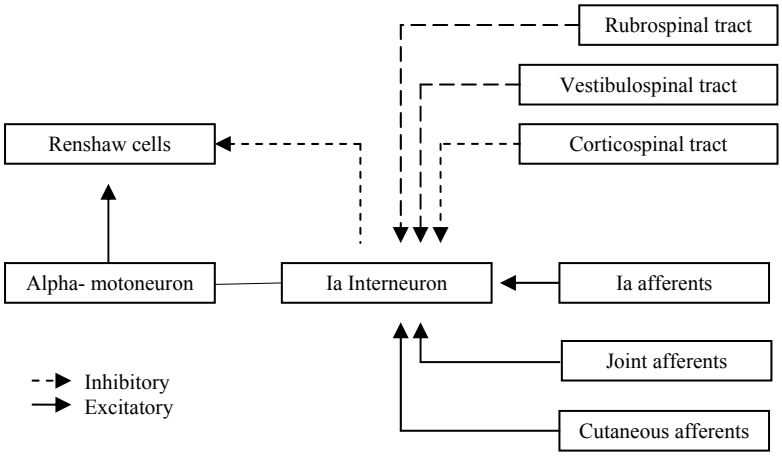


Figure 8. Schematic illustration of peripheral and central activity of the Ia inhibitory interneuron.

Ib Inhibitory Interneurons. The Ib inhibitory interneurons control movement through ascending and descending control (Figure 9). They receive action potentials from Ib afferent, Ia afferent, proprioceptors, cutaneous receptors, and synapse on alpha-motoneurons.[44, 157] They also receive excitatory input from the corticospinal tract, rubrospinal tract, and inhibitory input from the lateral reticulospinal tract.[157]

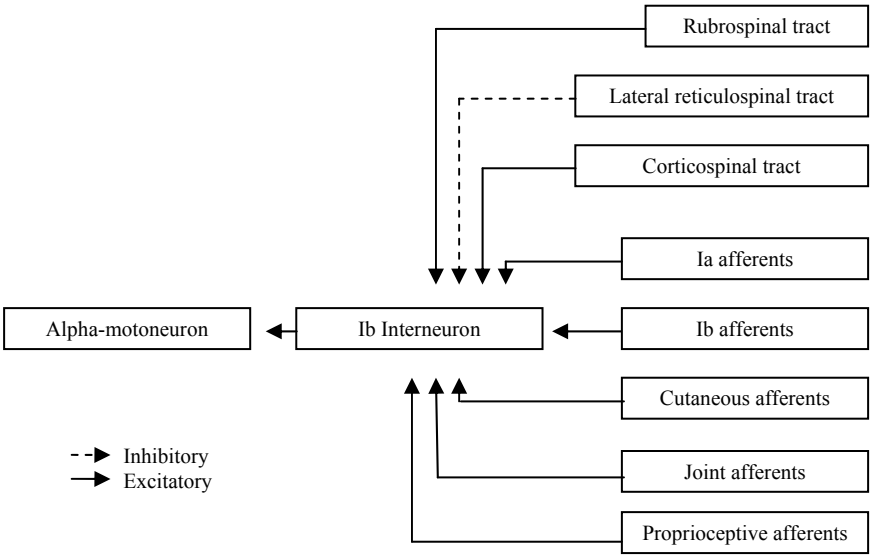


Figure 9. Schematic illustration of peripheral and central activity on the Ib inhibitory interneuron.

Renshaw Cells. Renshaw cells are inhibitory interneurons located in the ventral horn of the spinal cord (Figure 10).[44] They inhibit the alpha-motoneuron that activate Renshaw cells, motoneurons in the motoneuron pool, and the Ia inhibitory interneuron, which normally inhibits antagonistic muscles. Renshaw cells also receive excitatory and inhibitory action potentials from the lateral corticospinal tract and the ventral spinocerebellar tract.

Renshaw cells decrease or remove inhibition (disinhibition) of agonist and antagonistic muscles around a joint, causing co-contraction. This co-contraction acts to stabilize a joint during movement.[44] Investigators examining cats reported spinal interneurons that excite Renshaw cells also excite the motoneurons parallel to those Renshaw cells (i.e. other Renshaw cells). If this observation is the same in vivo, increased excitability via a pain stimulus may cause excitation of Renshaw cells and

inhibit adjacent alpha-motoneurons, gamma-motoneurons, or Ia inhibitory interneurons. This process of Renshaw cell activity is called recurrent inhibition.

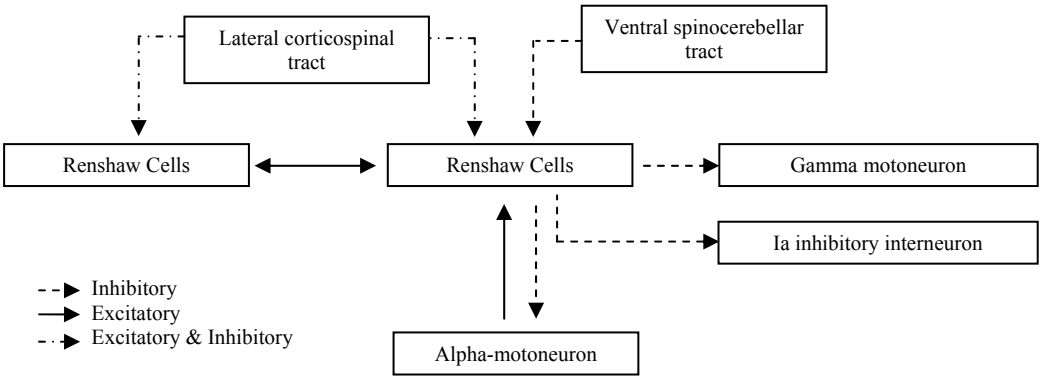


Figure 10. Schematic illustration of peripheral and central activity of Renshaw cells.

MEASURING MOTONEURON ACTIVITY

Electromyography

Electromyography (EMG) is a tool used to measure action potentials as they propagate along the sarcolemma to the neuromuscular junction of individual muscle fibers.[32] It is used to diagnose neurological disorders in the neuromuscular system and by scientists examining neuromuscular physiology.[32]

Electromyography captures changes in voltage associated with the propagation of action potential through electrodes. Electrodes vary in material and size. For example, there are surface electrodes and fine wire electrodes. Surface electrodes consist of large (30 cm^2) rubber-carbon pads, sponge pads, and silver-silver chloride (Ag-AgCl) disks. Fine wire electrodes (25 μm in diameter) are constructed from small diameter, highly nonoxidizing stiff metals, such as silver and nickel-chromium alloys with insulation or

platinum alloys.[32] Fine wire electrodes are advantageous when the area of interest is in a localized area of a muscle such as small muscles. The disadvantage of using fine wire electrodes is that they are not representative of the whole muscle. In addition the reliability coefficients are lower for wire electrodes than surface electrodes, the required implantation of the wires by needle insertion might be impractical or painful to the subject, and if the subject moves while the electrodes are inserted into a muscle the electrode could possibly break.[32]

Surface electrode application is crucial for accurate EMG signaling. In order to achieve the best results, skin must be appropriately prepared to reduce impedance. There are two methods of reducing impedance: 1) remove skin hair with a razor, dead epidermal skin cells with fine sand paper, and cutaneous oil with isopropyl alcohol or 2) shave the skin with a razor and apply an abrasive skin prepping gel. Supposedly, cleansing the skin with alcohol alters the electrical activity thus the recommended method of application is the abrasive skin prepping gel. This gel contains an abrasive material (fiber glass) that removes dead epidermal skin without altering the electrical activity (personal communication, Takieo Fujiwara Ph.D, MD).

Surface electrodes must have a contact medium such as water or hypoallergenic ultrasonic gel to work.[32] In addition, each surface electrode must be maintained in the same location during an experiment. Changing an electrodes position may have a significant impact on the EMG results.[32] Therefore, care must be taken when applying surface electrodes to the skin.

The greatest EMG amplitude is obtained by using a bipolar electrode configuration. Two EMG electrodes are placed in a longitudinal fashion near the center of the muscle being tested. The electrical activity recorded by each electrode is transmitted to an EMG machine that filters, processes, and amplifies the signal of each electrode.[32]

Hoffman Reflex

The H-reflex was originally described by Paul Hoffmann in 1910[25, 160] and later given his name.[161] It is a tool used to estimate the level of alpha-motoneuron pool activation.[25] It is done by eliciting a monosynaptic reflex conveyed by the Ia sensory fibers.[25] Measuring the H-reflex is relatively simple procedure that can be used to estimate the effect of various interventions on motoneuron pool activity (e.g. the injection of a pain stimulus).[22]

H-reflex and M-response. To elicit an H-reflex, a percutaneous electrical stimulation is delivered to a superficial mixed peripheral nerve.[25] Beginning with a low intensity, stimuli are gradually increased. This gradual increase results in the depolarization and the propagation of action potentials along Ia afferent nerve fibers to the spinal cord. If these action potential are sufficient to cause depolarization at the Ia-alpha-motoneuron synapse, neurotransmitters are released from the presynaptic nerve endings and moved across the synaptic cleft where they bind to specific receptors on the postsynaptic ending of alpha-motoneurons. Once the neurotransmitter binds to the postsynaptic membrane, an action potential causes acetylcholine (ACh) to be released, muscle contraction occurs, and an H-reflex appears as measured with EMG.[25]

H_{max} and M_{max}. During H-reflex measures, stimulus intensity is increased to a maximum H-reflex (H_{max}). H_{max} is an estimate of the number of motoneurons capable of being recruited. Once H_{max} is achieved, any additional increase causes a decline and eventual disappearance of the H-reflex (antidromic collision) and an increase in a motor response. The motor response (M-response) represents motoneuron pool activation. Maximum M-response is referred to as M_{max}. M_{max} theoretically represents the level of motoneuron pool activation.[161] This increase and decrease of the H-reflex and M_{max} is represented in the Figure 11.[25]

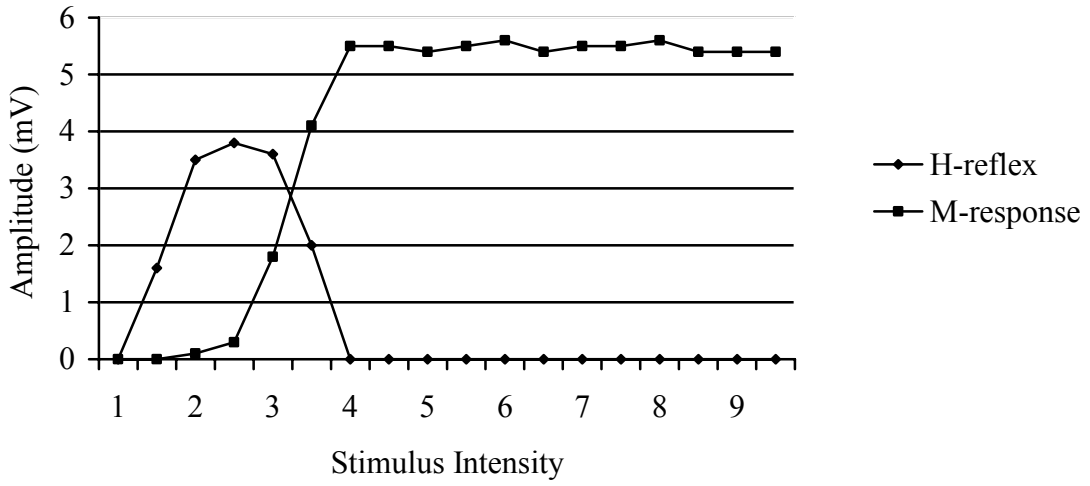


Figure 11. H-reflex and M-wave recruitment curve. The stimulus intensity set at 0 and gradually increased until H_{max} amplitude and maximum motor response (M_{max}) are achieved. Adopted from Palmieri et al.[25]

Antidromic collision occurs when motor fibers depolarize and convey action potentials toward the neuromuscular junction (orthodromic conduction) and to the spinal cord (antidromic conduction). Antidromic conduction from motor axons causes

depolarization of the alpha-motoneuron right before the Ia afferent neurons are able to depolarize. Depolarization as a result of antidromic conduction places the alpha-motoneurons in a refractory period resulting in the inability to respond to action potentials from the Ia afferent neurons.[153]

H:M_{max} Ratio. Standardizing the H_{max} amplitude to the M_{max} amplitude is a commonly used method of H-reflex normalization.[25] Since H_{max} represents an estimate of the number of motoneurons that are available to be recruited and the M_{max} represents the number of motoneurons in the motoneuron pool that are activated, the H:M_{max} ratio is the proportion of the motoneuron pool capable of being recruited.[25] In order for this method of normalization to be true, the M_{max} must be stable. Previous investigators have reported change in M_{max} over the course of their investigation.[162] Reasons for these changes include movement of the stimulating electrode or movement of the EMG electrodes. It is recommended that the M_{max} remain stable after each measurement so that any changes in M_{max} amplitude may be accounted for.[25]

Subject Positioning. Subject position is essential during the H-reflex testing.[25] Factors such as eye closure,[163] head position,[163] joint position,[164, 165] and muscle contraction[163] can affect the H-reflex amplitude.[25] Body position for H-reflex is a semi-reclined position,[166] supine position,[10, 156, 167-171] or standing position,[167] with the head, arms, and legs in a stable and relaxed position.

H-reflex Delivery. Low intensity 1 mS stimuli delivered to a superficial nerve produces the H-reflex. Careful attention, however, must be paid to the frequency of the stimuli delivered. Stimuli that are too close together will decrease the H-reflex

amplitude.[172] This decrease is caused by previous activation in Ia afferent and the depletion of neurotransmitter available. By performing too much stimulation in a short amount of time postactivation depression may occur. Stimuli applied at least 10 seconds apart however, will reduce the effects of postactivation depression.[173] Post activation depression may occur following previous activation of the Ia-motoneuron.. When the Ia afferent synapses with the motoneuron decreased neurotransmitters are released resulting in inhibition of the reflex pathway. This depression associated with the inhibition is hypothesized to be involved with pre-synaptic mechanisms.[174]

H-reflex Electrode Placement. Bipolar surface Ag-AgCl pregelled electrodes spaced ~ 2 cm apart is the most common setup for H-reflex measures. Changing the muscles' position during the experiment can alter the H-reflex measure without affecting the neural drive to the muscle.[25] Therefore, caution should be taken when interpreting H-reflex data in which there are changes in muscle position.

VOLUNTARY FORCE PRODUCTION

Maximal voluntary isometric contraction (MVIC) is the maximal isometric force a individual is able to produce.[175] During investigations of human skeletal muscle function involving maximal voluntary isometric contraction (MVIC), it is often assumed there is complete skeletal muscle activation.[176] Two methods to asses skeletal muscle activation are the interpolated twitch technique (ITT) [175, 177-189] and central activation ratio (CAR).[176, 190-193]

Interpolated twitch technique (ITT) was first used by Merton[183] to observe muscle inactivation. He superimposed an electrical stimulation while subjects were performing a

MVIC and an identical superimposed stimulus at rest.[179, 183, 190] Since Merton other investigators have used ITT to assess skeletal muscle activation of the dorsiflexors,[180] quadriceps,[178, 181, 187] plantarflexors,[179, 180] and elbow flexors.[182] It is calculated as

$$\mathbf{ITT} = \left(\mathbf{1} - \mathbf{superimposed\,stimulus\,torque\,/\,resting\,stimulus\,torque}\right) \times \mathbf{100}$$

Central activation ratio (CAR) is similar to the ITT method; however the superimposed stimulation is only delivered while a subject is performing a maximal voluntary isometric contraction. Numerous investigators used the CAR method[176, 184, 190-195] during activity involving skeletal muscle failure.[176] It is calculated as

$$\mathbf{CAR} = \left(\mathbf{MVC\,torque\,/\,MVC\,torque} + \mathbf{superimposed\,stimulus\,torque}\right) \times \mathbf{100}$$

Interpolated Twitch Technique vs. Central Activation Ratio

In Merton's description of ITT, he delivered a single superimposed stimulus during a MVIC and another superimposed stimulus at rest.[183] In more recent studies,[178, 189, 196] investigators reported two or more stimuli should be delivered because changes in force are more readily detected.[189] Two concerns with ITT are patient comfort and measurement sensitivity. Anecdotally, patients receiving the ITT experience more pain when the superimposed stimulus is delivered at rest. This pain may prevent an individual from producing maximal force with repeated trials. It is also reported that a superimposed single or double stimulus is more tolerable than a train of stimuli; however, the single and double stimuli may significantly underestimate a MVIC.[176] It is therefore recommended that a train of superimposed stimuli with the CAR be delivered. Superimposing a supramaximal train of stimuli during a MVIC provides a better measure of total force a muscle is capable of producing, and is more accurate.[176]

Central Activation Ratio Setup. Setup for CAR involves electrodes being placed over the polar-regions (motor regions) of the muscle/s or muscle belly. The patient then performs a MVIC where a stimulus is delivered to the muscle approximately 3 to 4 seconds into the contraction. This delay is due to anecdotal evidence where subjects report that they have not exerted maximal effort at the time of stimulation. During the measures, if the muscle being tested is fully activated, no additional force is produced by the electrical stimulation. If, however, all motor units are not activated, the stimulus will reveal a change in skeletal muscle activation.[176, 195]

Delivery for CAR varies between studies. In one investigation patients receiving total knee arthroplasty performed a 3 to 5 second MVIC while receiving verbal encouragement from the tester and visual feedback from a computer display screen. During contraction the subjects received a 100 mS train of 10 pulses at an intensity of 135 volts, with a frequency of 100 pulses per second to assess whether the subject was maximally activating the quadriceps muscle.[192] In another investigation, a 100 mS train of 10 square-wave pulses at an intensity of 125 volts with a 600 mS delivery at a frequency of 100 pulses per second in uninjured healthy subjects was used.[191]

Subject Familiarization. Subjects who are not familiar with MVICs are typically unable to perform consistent data that resemble a marked plateau in force production. Inadequate familiarization will therefore produce inconsistent data. Some subjects who are not familiar to the technique perform weaker contractions when the stimulus is expected rather than when it is not expected. One explanation for this may be that subjects are intimidated by the superimposed stimulus. In order to decrease the potential

weakness, subjects should be allowed to perform some MVICs with and without stimulation during a familiarization session.

CRYOTHERAPY AND NEUROPHYSIOLOGY

Under normal neurological conditions, nerve cells at rest are polarized, meaning that they possess a negative electrical charge.[197] This negative electrical charge is caused by the negative polarity inside the cell (intracellular space) and positive polarity outside the cell (extracellular space). This electrical potential difference between the intra- and extracellular space is referred to as the resting membrane potential.[33]

Resting membrane potential is maintained by three ions and two ion channels. The three ions are sodium, potassium, and chloride. Sodium and chloride are predominately located in the extracellular space with concentrations of 150 mM and 110 mM, respectively (intracellular concentrations are 15 mM and 10 mM, respectively). Potassium is predominantly located in the intracellular space with a concentration of 150 mM and an extracellular concentration of 95 mM.[50] The net difference for these ions in the intra- and extracellular space results in a resting membrane potential of approximately -70 mV[50] to -90 mV.[33, 198]

The two ion channels are the resting and gated channels. The resting channels are normally open and not influenced by the electrical potential difference between the intra- and extracellular space. The gated channels are closed when the cellular membrane is at rest and open when ions are being pumped from the intra- or extracellular space. At rest, sodium, chloride, and potassium move between the intra- and extracellular space by diffusing through the resting channels. This movement, however, can not occur for an

extended period of time because constant fluctuations of both sodium and potassium would eventually decrease the resting membrane potential. During unequal fluctuations of sodium and potassium ions, the gated sodium and potassium channels are activated. For example, if too many sodium ions diffuse through the resting channels and into the intracellular space, the sodium gates expel excess sodium in order to maintain sodium equilibrium within the extracellular space. Whereas, if too many potassium ions diffuse through the resting channels and into the extracellular space, the potassium gates expel excess potassium in order to maintain potassium equilibrium in the intracellular space.[33]

At rest this balance between sodium and potassium concentrations remains constant until the membrane reaches threshold. Threshold is reached when the outward diffusion of potassium is exactly equal to the inward diffusion of sodium[50] or when any stimulus causes a change in the resting membrane polarity.[33] Regardless of the mechanisms that initiate threshold, once threshold is achieved the cell membrane depolarizes. Depolarization is the rapid influx of sodium ions inside the intracellular space. This rapid influx is driven by the gated sodium channels. As sodium ions are actively moved inside the intracellular space, the intracellular space becomes less negative (more positive). As this area becomes less negative, more sodium gated channels open resulting in a greater depolarization. This depolarization continues until the electrical potential in the intracellular space reaches an equilibrium potential of +55 mV.[41] Once equilibrium potential is reached, the intracellular membrane begins to repolarize. Repolarization occurs when sodium channels begin to close (a process called

inactivation) and potassium gated channels open causing an influx of potassium ions into the intracellular space.[41]

This process of opening and closing both sodium-gated and potassium-gated ion channels is referred to as the nerve action potential. Nerve action potentials are self-propagating electrical signals that travel along the entire length of a nerve axon. Nerve action potentials are also all-or none, meaning that once threshold is reached the entire action potential occurs.

The effects of temperature on electrical activity have been studied since the early 1900s.[199] In one study temperature decreases between 3ºC and 20ºC altered resting membrane potential in a giant squid axon. However, following a stimulus causing nerve depolarization, temperature slowed down both opening and closing of sodium channels, where channel closing slowed down more than opening.[199] Channel closing being slower than opening would mean sodium channels are open longer. If sodium channels are open longer, more sodium ions can enter the intracellular membrane. This increase in sodium ion concentration inside the intracellular space could increase the rate or cause faster depolarizations. Faster depolarization could ultimately cause faster action potentials whereas faster action potentials could cause an increase in nerve conduction velocity. This action potential activity following temperature decreases is supported by Hodgkin and Katz.[199] They report at 35ºC resting membrane potential was 38 mV and action potentials were 46.5 mV. At 5ºC resting membrane potential was 47.5 mV and the action potentials were 85 mV, an increase of 37.5 mV as compared to resting membrane potential.[199]

Decreases in temperature influence the absolute and relative refractory periods. The absolute refractory period is the time during depolarization where all sodium channels are open and are incapable of responding to any stimulus. Therefore, if a decrease in temperature keeps the sodium channels open longer, it is possible that the absolute refractory period would be lengthened. In addition, the relative refractory period would also be increased. The relative refractory period is the point where all sodium gates are closed and the potassium gates are opening, thus initiating intracellular repolarization. During this repolarization, if an exceptionally strong stimulus causes the membrane to reach threshold, the sodium gates open resulting in another action potential. [50] Therefore, if the sodium gates are open and a decrease in temperature lengthens the refractory period it is possible the relative refractory periods would be lengthened. This data is supported by Lowitzsch et al. [200] They reported that cold application increased the absolute refractory period from 0.54 mS at 35°C to 3.07 mS at 20°C and the relative refractory period from 3.19 mS to 20.09 mS at the same temperatures, respectively.

Decreases in temperature also influence motor unit action potentials (MUAP). Motor units consist of efferent axons exiting the anterior horn of the spinal cord, terminal branches, and the synapse between the terminal nerve branches and individual muscle fibers (neuromuscular junction). In a review by Rutkove[198] he hypothesized that cooling a muscle may decrease action potential velocity in terminal nerve branches. This decrease in velocity would then lengthen the action potential duration. This hypothesis was partially observed by Buchthal et al.[201] in 1954. They reported an increase in biceps

MUAP with different levels of cooling. For example, MUAP at 37ºC increased 3%, at 30ºC increased 10-15%, and at 24-25ºC the increase was 30-45%.

Muscle spindles are influenced by decreases in temperature. Eldred et al[202] reported that a 10-15ºC decrease below normal rat body temperature as measured with a thermocouple inserted into muscle, decreased annulospiral endings (primary afferents) approximately 56%, type II afferents decrease approximately 42%, and Golgi tendon organs decreased approximately 50%.

Cryotherapy and H-reflex

Numerous investigators have examined cryotherapy and involuntary motoneuron pool excitability using the H-reflex.[9, 10, 203, 204] Cryotherapy disinhibits and facilitates motoneuron pool activity during and up to 30 minutes following an effused knee joint. The mechanism of how cryotherapy disinhibits and facilitates the motoneuron activity is not known. However, disinhibition may be attributed to decreases in sensory nerve conduction velocity[95] and discharge rate of mechanoreceptors located in skeletal muscle.[202] Following the removal of ice, cooling continues to decrease tissue temperature for up to 30 minutes.[9] As tissue temperature decreases sensory nerve conduction velocity and the discharge rate of mechanoreceptors decreases the number of action potentials ascending to the spinal cord, ultimately decreasing (removing) inhibition (disinhibition).[10]

Facilitation may be attributed to increased activation of the cutaneous and joint receptors via ice bag application. By activating cutaneous and joint receptors, ascending action potentials are stimulating the release of neurotransmitters that activate Ia

interneurons, resulting in excitation of the motoneuron pool. It is also possible that increased motoneuron pool excitability following intervention (i.e. joint effusion or experimental pain) with concurrent ice application creates an environment were supraspinal activity may be involved.

When investigating cryotherapy and H-reflex previous investigators have used a sham ice bag that is approximately the same size and weight of a 1 kg ice bag. These sham ice bag which typically consists of a cat litter bag, should remain "thermal neutral.[10] In one investigation, it was reported that a sham ice bag (cat litter) increased skin surface temperature from 30.3 ± 0.5°C to 30.9 ± 0.7°C an approximate change of 0.6°C.[205] This temperature however was not maintained during a 10-minute postapplication period. In pilot work we examine if white rice application kept skin temperature at a "thermal neutral" temperature. We, however, observed that white rice application caused an increase in skin surface temperature from 29.98 ± 1.3°C to 2.29 ± 1.3°C an approximate change of 0.7°C. Although there was no significant temperature change observed between the cat litter application and the white rice application (0.1°C), cat litter will be used as our control variable in these experiment.

Cryotherapy and Voluntary Motor Output

Muscle contraction occurs when acetylcholine (Ach) is released from the axonal terminal and binds to its ACh receptors. These ACh receptor interactions initiate action potentials which are then propagated along the sarcolemma and down T-tubules. As this action potential moves down the T-tubules it stimulates the release of calcium ions from the terminal cisternae (located in the sarcoplasmic reticulum). Calcium ions bind to

Troponin C causing tropomyosin to go through a conformation change where it moves off the actin binding sites. Once tropomyosin moves, myosin heads bind to actin. This process continues as long as calcium is available.[197]

Reports on the effects of cryotherapy and voluntary motor output vary. Authors have reported increases,[206, 207,10, 208] decreases,[198, 209, 210] and no change[211, 212] in force following joint or muscle cooling. Furthermore, functional exercises such as shuttle run or vertical jump decrease,[213] or are unaffected[214] by cold application. In addition, peak vertical ground reaction force, during a vertical jump decreased following ice bath immersion.[215] These differences in motor output following cryotherapy may be attributed to type of measurement, location of application, type of cold treatment, or the time at which the voluntary motor output measurements were taken.[10]

Cryotherapy and Pain

The benefits of cryotherapy for sports injuries are well documented. In 1881 cold compresses were first recognized as an adjunct to decreasing pain [216] Cold decreases pain so that patients are able to perform rehabilitation that may not have been possible prior to the cryotherapy treatment.[1-3] In one study, patients treated with cryotherapy following orthopedic surgery experienced fewer postsurgical complications than those not treated with cryotherapy.[5] In another study, patients treated with ice packs had a significant reduction in the need for supplementary analgesic medication following different orthopedic operations.[5-7]

One problem with cold application however, is cold causes some pain before it decreases pain.[217] During an initial cold application, it is reported that patients

experience cold induced pain, however, these patients quickly habituate to the cold application in one to two cold treatments.[95, 217] For example, following a 20-minute cold immersion, subjects report an ~1.4°C decrease in pain following repeated cold immersions.[217]

In essence, the ability for cold to decrease injury pain is universally accepted,[6, 218] regardless that it may initially cause pain. The specific mechanism on how cryotherapy decreases pain, however, is not known. It is possible cryotherapy decreases pain due to:

- Decreased nerve conduction velocity of free nerve endings (A-delta and C-fibers)[219]
- Reduced metabolism in tissue[220]
- Raises patients pain threshold[219]
- Acts like a counterirritant[221]
- Causes the release of endogenous opioids[222]
- Inhibits spinal neurons[223]

Although cryotherapy has an influence on pain reduction, it is possible that the application of a substance that does not extract heat from the body may influence pain. In pilot work we noticed that the application of white rice caused and increase in pain during a 25-minute infusion of 5% hypertonic saline. Therefore, it is possible that the application of a substance similar in size to an ice bag may move the 5% saline around the knee resulting in the increased activation of peripheral A-delta and C fiber nociceptors. A sham ice bag will therefore be applied in our control group.

Chapter 3

METHODS

Two experiments will be conducted to answer 6 research questions (Table 1).

The following 4 conditions will be used in the experiments.

A. Saline infusion/cryotherapy
B. No saline infusion/cryotherapy
C. Saline infusion/sham (cat litter)
D. No saline infusion (needle stick)
E. Saline infusion

Table 1. Research questions to be answered using 5 treatment combinations in 3 experiments

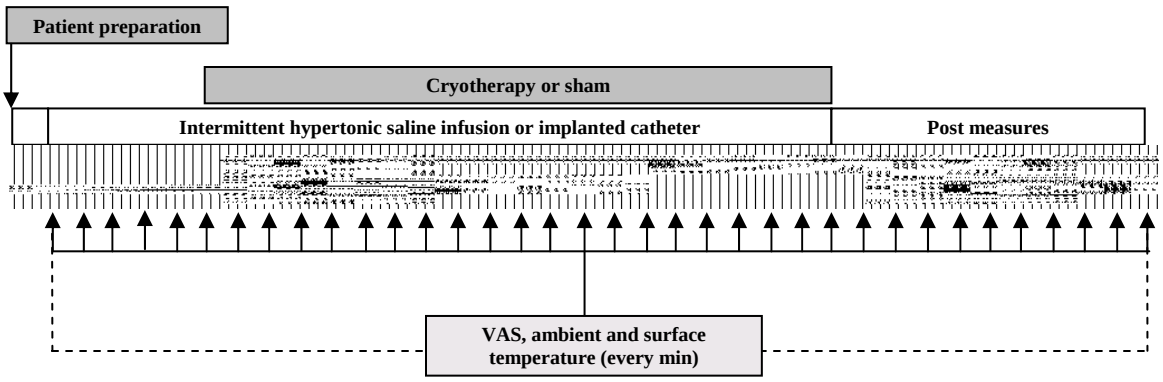
Research questions	Conditions
Experiment I. Variables: pain perception	
1. Does an intermittent infusion of 5% hypertonic saline into the infrapatellar fat pad cause consistent pain? - Answered by C	A. Saline infusion/cryotherapy B. No saline infusion/cryotherapy C. Saline infusion/sham
2. Does a 20-minute cryotherapy application during a 25-minute intermittent infusion of 5% hypertonic saline into the infrapatellar fat pad decrease pain? - Answered by A vs. B vs. C	
Experiment II. Variables: pain perception (McGill pain questionnaire) and Visual analogue scale, and H:M_{max} ratio	
3. Does a 20-minute infusion of 5% hypertonic saline into the infrapatellar fat pad cause AMI? - Answered by A vs. D	A. Saline infusion/cryotherapy C. Saline infusion/sham D. No saline infusion E. Saline infusion
4. Does a 20-minute cryotherapy application with a 20 minute intermittent infusion of 5% hypertonic saline into the infrapatellar fat pad alter motoneuron pool recruitment? - Answered by A vs. C vs. D	
5. Does a 20-minute sham ice bag application with a 20-minute intermittent infusion of 5% hypertonic saline into the infrapatellar fat pad alter pain? - Answered by A vs. C vs. D vs. E	
6. Does a 20-minute sham ice bag application with a 20-minute intermittent infusion of 5% hypertonic saline into the infrapatellar fat pad alter motoneuron pool recruitment? - Answered by C vs. D vs. E	

Study Designs

Experiment I. A 3 x 36 randomized controlled laboratory study with repeated measures on time will guide data collection. Independent variables will be condition [(saline infusion/ cryotherapy (saline/cryo), no-saline infusion/cryotherapy (no-saline/cryo), and saline infusion/sham (saline/sham)] and time (every minute during a preapplication (6), application (20) and for 10 minutes postapplication (10)). The dependent variable is perceived pain (visual analogue scale; VAS). Additionally, to determine if the same level of cooling in the cryotherapy conditions, and that temperature remains constant for the saline/sham condition, patella and popliteal surface temperatures will be measured every minute during preapplication, application, and postapplication.

Figure 12. Data collection Timeline for Experiment I

Independent Variables:	**Dependent Variables:**	**Control Variable:**
Condition (saline infusion/cryotherapy, no saline infusion/cryotherapy, saline infusion/sham) Time (precondition (6), every min during a condition (20), & for 10 min postcondition(10))	Pain perception (VAS)	Surface temperature



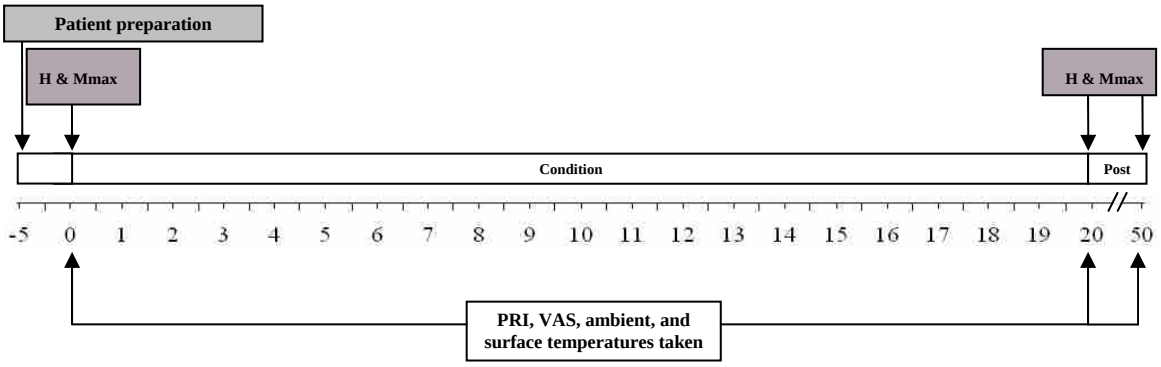
Experiment II. A 4 x 56 (treatment x time) randomized controlled laboratory study with repeated measures on time will guid this experiment. Independent variables will be treatment (saline infusion (saline), saline infusion/cryotherapy (saline/cryo), saline infusion/sham (saline/sham), and no-saline infusion (no-saline)) and time (pretreatment (pre), immediate posttreatment ($post_{tx}$), and 30-minutes posttreatment (30 min $post_{tx}$)). Measured dependent variables will be H_{max}, M_{max}, McGill Pain Questionnaire (MPQ), and pain perception (visual analogue scale; VAS). Additionally, to ensure the temperature remained constant in the noncryotherapy treatment and to know the level of cooling in the saline/cryo treatment, patella and popliteal surface temperatures will be measured every minute during preapplication, application, and postapplication.

Figure 13. Data collection Timeline for Experiment II

Independent Variables:
Group (saline infusion, saline infusion/cryotherapy, saline infusion/sham, no saline infusion)
Time (pre, $post_{tx}$ 30 min $post_{tx}$)

Dependent Variables:
McGill pain questionnaire
Pain perception (VAS)
$H:M_{max}$ ratio

Control Variable:
Surface temperature



Subjects

Seventy physically active college-age male volunteers will be recruited to participate in these investigations (30 in Experiment I and 40 in Experiment II). Each subject will be given a preparticipation health history questionnaire (Appendix A) to ensure that they are free of any neurological, cardiovascular, endocrine, or lower extremity orthopedic conditions. Subjects who are free from any of the above conditions will give written informed consent prior to their participation.

Instruments

Pain will be induced by a 24 GA x 0.75 in (0.7 x 19 mm) Teflon catheter (Alliance Medical, Russellville, MO) and simultaneous infusion of 5% hypertonic saline (B. Braun Medical, Inc., Irvine, CA). To infuse hypertonic saline, a 30 cm connection tube (B. Braun Medical, Inc, Bethlehem, PA) will be interfaced between the Teflon catheter and a 5 cc syringe filled with 5% hypertonic saline. The syringe will be positioned in a constant infusion pump (Harvard Apparatus, Millis, MA; model # 975) with an infusion range of 0.0004 to 8.0 cc/minute. A second 5 cc syringe filled with hypertonic saline will be used once the first syringe is completed.

For Experiment I, pain perception will be measured with a 100 mm VAS labeled "no pain" on the left polar end and "unbearable pain" on the right polar end.[26] For Experiment II, pain perception will be measured using a MPQ and a 100 mm VAS with the same labels on each polar end.[27]

For Experiment II, skin will be debrided with skin prepping gel (Nuprep, D.O. Weaver & Co., Aurora, CO). H-reflex measures will be collected using a stimulus

isolation adaptor (STMISOC, BIOPAC Systems, Inc., Santa Barbara, CA) connected to a shielded bar electrode (EL503, BIOPAC Systems, Inc., Santa Barbara, CA) to deliver stimuli. Surface pregelled Ag-AgCl self-adhesive disk electrodes (EL 503-10; BIOPAC Systems, Inc., Goleta, CA) separated from each other by 2 cm will be applied to the vastus medialis muscle. Signals from the surface electrodes will be amplified with a Telemetry unit (TEL100M, BIOPAC Systems, Inc., Santa Barbara, CA) and further processed with a BIOPAC EMG system (MP150, BIOPAC Systems, Inc. Santa Barbara, CA). Input impedance of the amplifier will be 2.0 MΩ, with a common mode rejection ratio of 110 dB, a signal/noise ratio of 65dB, and a gain of 1000. Raw data will be bandpass filtered at 10 and 500 Hz. A laptop computer will be connected to the EMG system to map all H- and M_{max} measures.

Surface temperature will be measured using 3 PT-6 Kapton insulated thermocouples (Physitemp Instruments, Inc., Clifton, NJ) interfaced to 3 channels in a 16-channel Iso-Thermex electrothermometer (Columbus Instruments, Columbus, OH). A desktop computer interfaced to the Iso-Thermex will be used to save all temperature measures. Temperature data will be recorded every minute throughout data collection.

Orientation

Subjects in Experiment I will go through a short orientation session held in the Brigham Young University Therapeutic Modality Laboratory before testing. The orientation will include an explanation of the experiment including the risks and benefits. Immediately following the orientation, subjects will be randomly assigned to 1 of the 3 conditions and then tested.

Subjects in Experiment II will go through a 30-minute orientation and screening session held in the Brigham Young University Therapeutic Modality Laboratory before testing. Orientation will include an explanation of the experiment including the risks and benefits. Subjects will then be screened to ensure they have a measurable quadriceps H-reflex and M-response. Subjects, who have the measurable responses, will be randomly assigned 1 of the 4 conditions. Once assigned, subjects will return back to laboratory at 48 or 72 hours from the screening day for testing. Those subjects without a measurable response will not be allowed to participate in the investigation.

Experimental Pain Procedures

Subjects will lie supine on a treatment table with their dominant leg (i.e. leg with which they kick a ball) slightly bent. A 2.5 X 2.5 cm area inferiolateral to the patella will be shaved and cleansed with povidone solution for catheter needle insertion. The catheter needle will be inserted into the cleansed area to a depth of 0.75 inches. Once inserted, the catheter needle will be extracted leaving the flexible Teflon catheter in the infrapatellar fat pad (Figure 14).

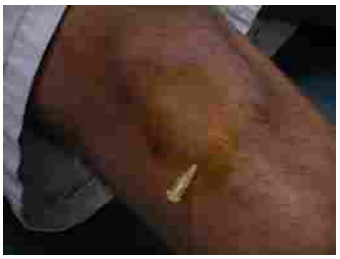


Figure 14. Teflon catheter inserted into the infrapatellar fat pad from the lateral side of the knee. The catheter will be inserted perpendicular to the patellar tendon.

The 30 cm connection tube will be interfaced between the Teflon catheter and 5 cc syringe filled with 5% hypertonic saline. The syringe will be positioned in the

constant infusion pump set to deliver the 0.54 cc of saline/minute. Saline infusion for Experiment I will last 25 minutes. Rate of saline delivery will be an on/off cycle of 3 minutes with the last minute being "on". Total volume of saline infused will be 7.02 cc. Saline infusion for Experiment II will last 20 minutes. Infusion rate will be 0.54 cc a minute during 4 consecutive on/off cycles. The on/off cycle will be 3 minutes with an exception of the last 2 minutes being "on". Total volume of saline infused will be 5.94 cc. Once the first 5 cc syringe is infused we will use a second 5 cc syringe filled with hypertonic saline.

H-reflex Procedure

Subjects will lie on their back with their dominant leg (i.e. leg with which they kick a ball) flexed to approximately 15° of knee and hip flexion. A 6 X 6 cm area over the vastus medialis and a 2.5 X 2.5 cm area over the tibial tuberosity will then be shaved and debrided with a skin prepping gel (Nuprep, D.O. Weaver & Co., Aurora, CO). Two surface electrodes will be applied to the greatest bulk of the vastus medialis as found during a maximal voluntary isometric contraction of their quadriceps. A ground electrode will be placed on the tibial tuberosity.

The stimulus electrode will then be placed over the femoral nerve in the femoral triangle of the dominant leg. To locate the femoral nerve, each subject's femoral pulse will be located. The electrode will then be placed just lateral to the femoral artery where the nerve is located. Once the electrode is placed over the femoral nerve, the subjects' heel will be placed in a polystyrene cube, designed to keep the heel stable and the lower extremity in a fixed position. The subjects will place their hands to their sides with their

palms up and hands open. They will be instructed to focus at a small picture on the ceiling, while listening to white noise through headphones. These steps will be used to decrease potential variability in the measurement and to maintain reliability.[169] Next, in order to find the best location over the femoral nerve with the stimulating electrode, a series of short duration (1.0 ms), high intensity (200 V max) stimuli will be delivered with varying amplitudes in order to find an H-reflex. Once the H-reflex is found, two double 6-inch elastic wraps will be used to hold the stimulating electrode in place. One elastic wrap will be placed over the stimulating electrode. The second elastic wrap will be wrapped around the subject's waist to stabilize the first elastic wrap over the femoral nerve.

Once the stimulating electrode is secured, another series of short duration (1.0 ms), high intensity (200 V max) stimuli will be delivered through the stimulating electrode with varying amplitudes in order to find the maximum H-reflex (H_{max}). These stimuli will be delivered in a trial-and-error method in order to find the peak H-reflex amplitude. Beginning with the lowest intensity, stimuli will be increased in 2-5 mA increments. With the stimulating amplitude set at the H_{max}, 5 measurements will be taken with a 20-second rest between measurements. The stimulus intensity will then be incrementally increased to find the maximum M-response (M_{max}) for normalization of the H-reflex. Once the M_{max} is set, 5 measurements will be taken with a 20-second rest between measurements.

Cryotherapy Procedures

Two polyethylene bags filled with 1-kg of crushed ice or cat litter will be secured to the anterior and posterior surfaces of the knee joint with a double length 6-inch elastic wrap. Temperature will be recorded with 1 thermocouple located in the: center of the patella and center of the popliteal fossa. For Experiment II, care will be taken so that the ice bags do not come in contact with the surface electrodes located on the vastus medialis muscle. Temperature measures at the EMG electrode site are essential so that changes in temperature do not influence the post application H-reflex measures.

Testing Procedures

Subjects will report to the Therapeutic Modality Laboratory dressed in shorts and a T-shirt. Upon arrival, subjects will be position on a treatment table where their skin will be prepped for thermocouple application, 5% saline infusion, and EMG electrode application (Experiment II only). A Teflon catheter needle will then be inserted into the cleansed area, where the needle will be extracted leaving the Teflon catheter in the infrapatellar fat pad. Individual procedures for both experiments are as follows:

Experiment I. Surface thermocouples will be applied as previously described. A baseline (preinfusion) pain perception measure will be recorded on a VAS. For subjects assigned to receive no saline infusion/cryotherapy the Teflon catheter will be inserted into their infrapatellar fat pad and the 1-kg ice bags will be applied at the 5th minute. For subjects assigned to receive saline infusion, the 30-cm connection tube will be interfaced between the implanted Teflon catheter and the 5 cc syringe positioned in the constant infusion pump. At the 5th minute during saline infusion, a 1 kg ice bag or 1 kg sham ice

bag will be applied to the anterior and posterior sides of the knee joint for 20 minutes. At the 20th minute, subjects will remain on the table for an additional 10 minutes. During the 20-minute condition and 10-minute postcondition period, pain perception will be measured on new VASs every minute. Immediately following the 10-minute postcondition period, the 30 cm connection tube will be disconnected from the Teflon catheter, the catheter will be extracted from the infrapatellar fat pad, and the area will be treated with antibiotic ointment and a Band-Aid.

Experiment II. Surface electrodes and thermocouples will be applied to the skin as previously described. A baseline (preinfusion) H-reflex and pain perception measure will be taken. The pain perception measure will be recorded on a MPQ pain questionnaire and a VAS. For subjects assigned to receive no saline infusion/no cryotherapy the Teflon catheter will be inserted into their infrapatellar fat pad while they are supine on a treatment table. For subjects assigned to receive the 5% hypertonic saline, the 30 cm connection tube will be interfaced between the implanted Teflon catheter and the 5 cc syringe positioned in the constant infusion pump. The 1-kg ice bags or 1-kg sham ice bags will be applied to the knee joint. Saline infusion with simultaneous ice bag application will last 20 minutes. Immediately following and 30-minutes following each condition, another set of H-reflex and pain perception (MPQ and VAS) will be measured. Following each 30-minute condition, the 30 cm connection tube will be disconnected from the Teflon catheter, the catheter will be extracted from the infrapatellar fat pad, and the area will be treated with antibiotic ointment and a Band-Aid.

Data Management and Analysis

Experiment I. Descriptive statistics will be computed for perceived pain (VASs), surface temperature at the patella and popliteal fossa, and ambient temperature. We will use four 3 X 36 (condition X time) mixed model ANOVAs with random effects for subjects and a within-subject order-1 autoregressive (AR-1) [224] correlations. Two of the AR-1 correlations will be used to determine if pain or surface temperature (patella and popliteal) changed between conditions across time. The other two AR-1 correlations will be used to determine if the subsequent pain or surface temperature measures change within each condition across time. All surface temperature data will be summarized by application phase.

We will use Tukey-Kramer post-hoc multiple comparison tests to examine individual differences in perceived pain and surface temperature. For all differences, the level of significance will be set at $P < .05$. Data will be analyzed with the MIXED procedures of Statistical Analytical Software (SAS; 9.1 Carey, North Carolina). Thermocouple uncertainty will be computed for the 3 thermocouples according to Jutte et al.[225].

Experiment II. We will comput means and standard deviations for $H:M_{max}$ ratio, PRI, VAS, and patella, popliteal, and ambient temperature pre, immediate $post_{tx}$ and 30 minutes $post_{tx}$. The mean of 5 H_{max} and 5 M_{max} measures will be calculated for the quadriceps $H:M_{max}$ ratio. Percent changes in $H:M_{max}$ ratio will also calculated. The PRI will be calculated by summing the numerical value for each word selected in the sensory,

affective, evaluative, and miscellaneous sections of the MPQ. Pain perception scores on the VAS's will be measured in millimeters from the left polar end.

Six 3 X 4 (time X group) mixed model analyses with repeated measure on time for will be used to examine differences for H:M_{max} ratio, PRI, VAS, patella and popliteal surface temperatures, and ambient air temperature.

Tukey-Kramer post hoc multiple comparison tests will be used to examine individual differences in perceived pain and temperature between groups at each time. For all differences, the level of significance will be set at $P < .05$. Data will be analyzed with the MIXED procedures of Statistical Analytical Software (SAS; 9.1 Carey, North Carolina). Thermocouple uncertainty will be computed for the 3 thermocouples according to Jutte et al.[226]

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Appendix B

Additional Methods

Figures

Table B 2. Subject Demographics, Randomization Group, and Tested Leg for Experiment I

Subject	Randomized assignment (#)	Knee	Age	Height (cm)	Mass (kg)
1	Saline/sham (3)	Left	25	185.4	74.1
2	No saline/cryo (2)	Right	25	177.8	33.7
3	Saline/sham (3)	Right	24	182.9	88.6
4	Saline/cryo (1)	Right	21	190.5	84.1
5	No saline/cryo (2)	Right	23	170.2	72.7
6	Saline/sham (3)	Right	21	190.5	118.2
7	Saline/cryo (1)	Right	23	172.7	68.8
8	Saline/sham (3)	Right	23	185.4	79.5
9	Saline/sham (3)	Right	18	180.3	79.5
10	Saline/cryo (1)	Right	22	177.8	72.7
11	Saline/sham (3)	Right	23	177.8	90.9
12	No saline/cryo (2)	Right	24	177.8	88.6
13	No saline/cryo (2)	Right	21	180.3	75.0
14	Saline/cryo (1)	Right	23	172.7	86.4
15	Saline/cryo (1)	Right	18	185.4	75.0
16	Saline/cryo (1)	Right	23	185.4	75.9
17	Saline/cryo (1)	Right	24	172.7	90.0
18	Saline/cryo (1)	Right	19	182.9	62.5
19	No saline/cryo (2)	Right	22	193.0	86.4
20	Saline/cryo (1)	Right	24	182.9	79.5
21	Saline/sham (3)	Right	21	175.3	74.1
22	Saline/sham (3)	Right	18	177.8	85.0
23	No saline/cryo (2)	Right	21	175.3	65.0
24	Saline/sham (3)	Right	22	188.0	84.1
25	No saline/cryo (2)	Right	22	185.4	109.1
26	Saline/sham (3)	Right	26	177.8	113.6
27	No saline/cryo (2)	Right	22	188.0	93.2
28	No saline/cryo (2)	Right	22	177.8	68.2
29	Saline/cryo (1)	Left	25	180.3	88.6
30	No saline/cryo (2)	Right	25	177.8	77.0

Table B 3. Subject Demographics, Randomization Group, and Tested Leg for Experiment II

Subject	Randomized assignment (#)	Knee	Age	Height (cm)	Mass (kg)
1	No saline/no cryo (4)	Left	22	188.0	93.2
2	Saline/cryo (2)	Right	18	180.3	75.9
3	No saline/no cryo	Right	22	185.4	72.7
4	Saline/no cryo (1)	Right	25	185.4	75.0
5	Saline/no cryo (1)	Left	23	177.8	79.5
6	Saline/cryo (2)	Right	22	152.4	81.8
7	Saline/cryo (2)	Right	25	188.0	84.1
8	No saline/no cryo (4)	Right	24	182.9	84.1
9	No saline/no cryo (4)	Left	24	182.9	70.0
10	Saline/no cryo (1)	Right	19	177.8	68.2
11	Saline/sham (3)	Right	23	182.9	100.0
12	Saline/cryo (2)	Right	24	180.3	86.4
13	Saline/sham (3)	Right	21	170.2	77.3
14	No saline/no cryo	Right	24	172.7	78.2
15	Saline/sham (3)	Right	24	177.8	75.0
16	Saline/cryo (2)	Right	23	177.8	77.3
17	Saline/no cryo (1)	Right	22	180.3	68.2
18	Saline/sham (3)	Right	22	180.3	75.0
19	Saline/cryo (2)	Right	18	185.4	75.0
20	Saline/no cryo (1)	Right	24	172.7	75.0
21	Saline/cryo (2)	Right	22	172.7	68.2
22	Saline/no cryo (1)	Right	18	190.5	75.0
23	Saline/sham (3)	Right	22	185.4	84.1
24	No saline/no cryo	Right	22	180.3	72.7
25	Saline/cryo (2)	Right	19	182.9	76.4
26	Saline/cryo (2)	Right	19	165.1	60.5
27	Saline/sham (3)	Right	18	188.0	82.3
28	Saline/no cryo (1)	Right	23	175.3	68.2
29	Saline/sham (3)	Right	23	182.9	63.6
30	Saline/no cryo (1)	Right	23	195.6	86.4
31	No saline/no cryo	Right	24	177.8	63.6
32	Saline/no cryo (1)	Right	23	185.4	77.3
33	Saline/sham (3)	Right	21	177.8	61.8
34	Saline/cryo (2)	Right	18	180.3	66.8
35	No saline/no cryo	Right	21	190.5	88.6
36	No saline/no cryo (4)	Right	23	180.3	87.7
37	Saline/sham (3)	Right	21	180.3	68.2
38	No saline/no cryo	Right	21	190.5	70.0
39	Saline/no cryo (1)	Right	18	185.4	77.3
40	Saline/sham (3)	Left	23	177.8	68.2

Table B 4. Pain Between Each Condition Across Time

```
PROC IMPORT OUT= WORK.d1
            DATAFILE= "C:\udrive\research\long\Raw Data.xls"
            DBMS=EXCEL REPLACE;
  SHEET="'Stacked Data$'";
  GETNAMES=YES;
  MIXED=NO;
  SCANTEXT=YES;
  USEDATE=YES;
  SCANTIME=YES;
RUN;

proc print data=d1;
run;

proc sort data=d1;
by condition subject time;
symbol l=1 i=join v=none repeat=100;
proc gplot data=d1;
by condition;
plot pain_measure*time=subject/vaxis=0 to 100 by 10;
run;

proc gplot data=d1;
where time ne 0;
by condition;
plot pain_measure*time=subject/vaxis=0 to 100 by 10;
run;
proc gplot data=d1;

options ls=120;
options ps=10000;
proc mixed data=d1;
title 'pain';
where time ne 0;
class subject time condition phase;
model pain_measure=condition|time;
random subject/group=phase;
repeated /subject=subject type=ar(1);
*lsmeans condition*time/pdiff adjust=tukey;
run;
```

Table B 5. Sequential Time Differences for Pain

```
PROC IMPORT OUT= WORK.d1
            DATAFILE= "C:\udrive\research\long\Raw Data.xls"
            DBMS=EXCEL REPLACE;
  SHEET="'Stacked Data$'";
  GETNAMES=YES;
  MIXED=NO;
  SCANTEXT=YES;
  USEDATE=YES;
  SCANTIME=YES;
RUN;

data d1;
infile 'C:\udrive\research\long\pain diff.txt';
input a $ t1 c1 t2 c2 diff sed df t p lab $ ap;
if c1=c2;
proc sort data=d1;
by c1 t1 t2;
proc print data=d1;
run;

data d2;
set d1;
if t2-t1=1;
proc print data=d2;
run;
data d1;
```

Table B 6. Change in Pain Following Each Measure on the VAS

```
PROC IMPORT OUT= WORK.d1
        DATAFILE= "C:\udrive\research\long\Raw Data.xls"
        DBMS=EXCEL REPLACE;
    SHEET="'Stacked Data$'";
    GETNAMES=YES;
    MIXED=NO;
    SCANTEXT=YES;
    USEDATE=YES;
    SCANTIME=YES;
RUN;

*proc print data=d1;
run;

data d2;
set d1;
lastpain=lag1(pain_measure);
diff=pain_measure-lastpain;
if verbal_response=2 then verbal_response=3;
if verbal_response=6 then verbal_response=5;
if verbal_response=. then diff=.;
better=(diff lt 0);
*proc print data=d2;
*where verbal_response=2;
run;
proc sort data=d2;
by condition verbal_response subject;
proc univariate data=d2 plot;
where verbal_response ne .;
by condition verbal_response;
var diff better;
run;
```

Table B 7. Patella Surface Temperature for Each Condition Within Each Phase

```
PROC IMPORT OUT= WORK.d1
            DATAFILE= "C:\udrive\research\long\Raw Data.xls"
            DBMS=EXCEL REPLACE;
  SHEET="'Stacked Data$'";
  GETNAMES=YES;
  MIXED=NO;
  SCANTEXT=YES;
  USEDATE=YES;
  SCANTIME=YES;
RUN;

proc print data=d1;
run;

proc mixed data=d1;
title 'patella temp';
class subject time condition phase;
model patella_temp=condition phase condition*phase condition*time(phase);
random subject;
repeated /subject=subject type=ar(1);
lsmeans condition*phase/pdiff adjust=tukey;
run;
```

Table B 8. Popliteal Surface Temperature for Each Condition Within Each Phase

```
PROC IMPORT OUT= WORK.d1
            DATAFILE= "C:\udrive\research\long\Raw Data.xls"
            DBMS=EXCEL REPLACE;
  SHEET="'Stacked Data$'";
  GETNAMES=YES;
  MIXED=NO;
  SCANTEXT=YES;
  USEDATE=YES;
  SCANTIME=YES;
RUN;

proc print data=d1;
run;

proc mixed data=d1;
title 'pop temp';
class subject time condition phase;
model popliteal_temp=condition phase condition*phase condition*time(phase);
random subject;
repeated /subject=subject type=ar(1);
lsmeans condition*phase/pdiff adjust=tukey;
run;
```

Table B 9. Ambient Room Temperature for Each Condition Within Each Phase

```
PROC IMPORT OUT= WORK.d1
            DATAFILE= "C:\udrive\research\long\Raw Data.xls"
            DBMS=EXCEL REPLACE;
  SHEET="'Stacked Data$'";
  GETNAMES=YES;
  MIXED=NO;
  SCANTEXT=YES;
  USEDATE=YES;
  SCANTIME=YES;
RUN;

proc print data=d1;
run;

proc mixed data=d1;
where ambient_temp gt 19;
title 'ambient temp';
class subject time condition phase;
model ambient_temp=condition phase condition*phase condition*time(phase);
random subject;
repeated /subject=subject type=ar(1);
lsmeans condition*phase/pdiff adjust=tukey;
run;
```

Table B 10. H:M_{max} Ratio for Each Condition Across Time

```
proc mixed data=d1;
title h_mratio analysis;
class subject condition time ;
model h_mratio=time|condition/outp=p1;
random subject;
lsmeans time*condition/adjust=tukey pdiff;
run;
*proc plot data=p1;
*plot resid*pred;
run;
```

Table B 11. PRI for Each Condition Across Time

```
proc mixed data=d1;
where time ne 0;
title pri analysis;
class subject condition time ;
model pri=time|condition/outp=p1;
random subject;
lsmeans time*condition/adjust=tukey pdiff;
run;
*proc plot data=p1;
*plot resid*pred;
run;
```

Table B 12. Patella Surface Temperature for Each Condition Across Time

```
proc mixed data=d1;
where time=0 or time=25 or time=55;
title patella_temp analysis;
class subject condition time ;
model patella_temp=time|condition/outp=p1;
random subject;
lsmeans time*condition/adjust=tukey pdiff;
run;
*proc plot data=p1;
*plot resid*pred;
run;
```

Table B 13. Pain Perception for Each Condition Across Time as Measured on the VASs

```
proc mixed data=d1;
where time ne 0;
title vas analysis;
class subject condition time ;
model vas=time|condition/outp=p1;
random subject;
lsmeans time*condition/adjust=tukey pdiff;
run;
*proc plot data=p1;
*plot resid*pred;
run;
```

Table B 14. Pain Perception for Each Condition Across Time as Measured on the PPI

```
proc mixed data=d1;
where time ne 0;
title ppi analysis;
class sub cond time ;
model ppi=time|cond/outp=p1;
random sub;
lsmeans time*cond/adjust=tukey pdiff;
run;
*proc plot data=p1;
*plot resid*pred;
run;
```

Table B 15. Pain Perception for Each Condition Across Time for Popliteal Surface Temperature

```
proc mixed data=d1;
where (time=0 or time=25 or time=55);
title pop_ analysis;
class sub cond time ;
model pop_=time|cond/outp=p1;
random sub;
lsmeans time*cond/adjust=tukey pdiff;
run;
*proc plot data=p1;
*plot resid*pred;
run;
```

Table B 16. Pain Perception for Each Condition Across Time for Ambient Room Temperature

```
proc mixed data=d1;
where (time=0 or time=25 or time=55);
title amb_ analysis;
class sub cond time ;
model amb_=time|cond/outp=p1;
random sub;
lsmeans time*cond/adjust=tukey pdiff;
run;
*proc plot data=p1;
*plot resid*pred;
run;
```

Figure B 1. Subject Information & Injury History Questionnaire for Experiment I and II

Please answer the following questions to the best of your knowledge. Please place a check in the appropriate box. All information from this questionnaire will be kept confidential.

Name: _____

Phone number: _____

Email: _____

Please indicate the most appropriate answer to the following questions	YES	NO
1. Do you have any known lower extremity neurological disorders?		
2. Do you have any loss of sensation?		
3. Do you have diabetes?		
4. Do you have any cardiovascular conditions?		
5. Are you currently taking prescription or over the counter medication for a neurological disorder or pain?		
6. Have you taken any stimulating substances such as caffeine within the last 24 hours?		
7. Do you know of or have any medical conditions that might aggravate you during the study?		
8. Are you experiencing any pain in your lower extremity at this time?		
1. Have you ever had an ice bag applied to an extremity? If yes: when was the last time you applied the ice bag_____ where was the ice bag applied_____ how long (min)was the ice bag applied_____ how many days, weeks, months was the ice bag applied _____		

Should you become ill and/or incapable of finishing the study, alert the investigator immediately and first aid will be administered.

You may withdraw from this study at any time without prejudice.

Figure B 2. Institutional Review Board Approval Letter for Experiment I

INSTITUTIONAL REVIEW BOARD FOR
HUMAN SUBJECTS

September 27, 2007

Blaine C. Long
117 RB
Campus Mail

Re: Does Cryotherapy Influence Experimentally Induced Pain?

Dear Blaine,

This is to inform you that Brigham Young University's IRB has approved the above research study.

The approval period is from **9/27/2007 to 8/1/2008. Your study number is F07-0268. Please be sure to reference either this number in any correspondence with the IRB.**

Continued approval is conditional upon your compliance with the following requirements:

- A copy of the **Informed Consent Document**, approved as of **9/27/2007** is enclosed. No other consent form should be used. It must be signed by each subject prior to initiation of any protocol procedures. In addition, each subject must be given a copy of the signed consent form.
- All protocol amendments and changes to approved research must be submitted to the IRB and not be implemented until approved by the IRB.
- **The enclosed recruitment advertisement has been approved.** Advertisements, letters, Internet postings and any other media for subject recruitment must be submitted to IRB and approved prior to use.
- A few months before this date we will send out a continuing review form. There will only be two reminders. Please fill this form out in a timely manner to ensure that there is not a lapse in your approval.

If you have any questions, please do not hesitate to call me.

Sincerely,

Dr. Renea L. Beckstrand, Chair
Sandee M.P. Muñoz, Administrator
Institutional Review Board for Human Subjects
RLB/se
Enclosures

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Figure B 3. Institutional Review Board Addendum Letter for Experiment I

INSTITUTIONAL REVIEW BOARD FOR
HUMAN SUBJECTS

October 24, 2007

Blaine C. Long
117 RB
Campus Mail

Re: Does Cryotherapy Influence Experimentally Induced Pain?

Dear Blaine,

This is to inform you that Brigham Young's University's Institutional Review Board has reviewed your addendum and recruiting flyer for the above captioned study. The changes to the study have been approved.

Please find revised Informed Consent document enclosed. You will note that the date of approval at the bottom right hand corner has been updated 10/24/2007 . No other consent form should be used. It must be signed by each subject prior to initiation of any protocol procedures. In addition, each subject must be given a copy of the signed consent form.

The approval period for the study ends on 8/1/2008. Any additional modifications in the research protocol, study site/ personnel, or consent form during this time period must first be reviewed and approved by the IRB.

If you have any questions, please let us know. We wish you well with your research!

Sincerely,

Christopher Dromey, PhD, Chair
Sandee M.P. Muñoz, Administrator
Institutional Review Board for Human Subjects
CD/se
Enclosures

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Figure B 4. Institutional Review Board Informed Consent to be a Research Subject for Experiment I

Revised document

Consent to be a Research Subject

Introduction

The purpose of these experiments is to determine if an ice bag influences your pain during the infusion of 5% saline. The study is being conducted by, Blaine C. Long MS, ATC (a graduate student), Kenneth L. Knight PhD, ATC, J. Ty Hopkins PhD, ATC, and Brent S. E. Rich, MD. You were selected to participate in this study because you are physically active, have not injured either leg in the last 6 months, have not had surgery on either leg in the last two years, are free of neurological, cardiovascular, endocrine (diabetes) conditions, and are not currently experiencing pain or consuming pain medication.

Procedures

You will report to the Therapeutic Modality Laboratory (Richards Building room 123) dressed in shorts and a T-shirt. You will read and sign this informed consent form and a health history questionnaire. Following your signature, you will be randomly assigned to 1 of 3 conditions. In order to determine which condition you will receive, you will pull a number 1, 2, or 3 out of a hat. The number you select will determine which condition (no saline infusion and ice application (1), saline infusion and ice application (2), no saline infusion and ice application (3) or saline infusion and sham ice bag.

You will lay on your back with your dominant leg (i.e. leg with which they kick a ball) bent. An area on the outside of your knee will be shaved with a razor and cleansed with an antiseptic oitment. Two skin thermometers will be applied. One thermometer will be applied to the front of your knee and the other will be applied to the back of your knee. If you are assigned to receive no saline infusion/ice application you will have the catheter inserted into the soft tissue outside of your knee joint and receive the 20 minute ice application. If you are assigned to receive saline infusion, a clear plastic tube filled with 5% saline will connect the catheter inserted in the soft tissue outside of your knee joint to a 5 ml syringe filled with 5% saline. Saline infusion will last for 25 minutes with a total of 7.02 ml infused. At the 5th minute during saline infusion a 1kg ice bag will be secured to the front and back of your knee with an elastic wrap for 20 minutes. At the 20th minute, the catheter will be removed from your knee, and you will remain on the table for an additional 10 minutes. During this 10 minute period, your wound from the catheter needle will be treated with Neosporin and a band aid.

Your pain will be measured using a 10 cm pain scale labeled "no pain" on the left end and "unbearable pain" on the right end. Your pain measurements will be taken before the catheter is inserted into the soft tissue outside of your knee joint, every minute during your condition, and for 10 minutes following your condition.

Risks

You will experience pain if you receive saline infusion. There is a slight possibility of tendon or knee joint injury during catheter insertion. To minimize risk of infection at the insertion site, an area on the outside of your knee will be thoroughly cleansed with antiseptic ointment (povidone). Immediately following the study the catheter will be extracted and Neosporin and a band aid will be applied. If any adverse affects were to occur as a result of the needle stick or if the tendon or joint capsule were to become injured during catheter insertion or saline infusion you will be examined by a Licensed Board Certified Athletic Trainer or a physician

Benefits

The benefits associated with this pain study are: 1) knowing a specific pain model that causes mild pain without long term affects. 2) Knowing a pain model to study the effects of cold on muscle activity. 3) Knowing how pain may contribute to skeletal muscle activation 4) Knowing that pain is a limiting factor in many peoples lives, each individuals contribution is advancing the knowledge of science in health care.

Confidentiality

All information provided will remain confidential and will only be reported as group data with no identifying information. All data including the questionnaire will be kept secured and only those involved in the study will have access to this information. Following the investigation, the questionnaires will be destroyed.

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Figure B 4. Continued

Compensation

If you complete the investigation, you will receive $30.00. However, if you do not complete the investigation, you will not receive compensation for your participation.

Participation:

Participation in this research study is voluntary. You have the right to withdraw at anytime or refuse to participate entirely without jeopardy to your class status, grade or standing with the university, etc.

Questions about the Research:

Do you have any questions (please circle one)? YES No

If yes, then write your question(s) on the back of this sheet and do NOT sign below until your questions have been answered satisfactorily. You may take as much time as necessary to think this over.

If you have any questions or comments regarding this study, you may contact:

Blaine Long MS, ATC, LAT	or	Kenneth L. Knight, PhD, ATC, FACSM
117 Richards Building		271 Smith Field House
Brigham Young University		Brigham Young University
(801) 422-9156		(801) 422-2984
blainelong@byu.edu		ken_knight@byu.edu

I have read, understood, and received a copy of the above consent, and desire of my own free will and volition, to participate in this investigation.

Questions about your Rights as Research Participants

If you have questions you do not feel comfortable asking the researcher, you may contact Christopher Dromey, PhD, IRB Chair, 133 TLRB, 422-6461, Christopher_dromey@byu.edu

I have read, understood, and received a copy of the above consent and desire of my own free will to participate in this study.

Signature:_____ Date:_____

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OCT 2 4 2007 - AUG 0 1 2008

Figure B 5. Research Opportunity Flyer for Experiment I

Research Opportunity

Volunteers are needed in this athletic training investigation. You qualify for this investigation if you are not allergic to ice and if you are free of any neurological, cardiovascular, endocrine (diabetes) conditions, and are not currently experiencing pain or consuming pain medication. You will be required to visit the **BYU Therapeutic Modality Laboratory (RB room 123)** 1 time for approximately 1.5 hours. If you decide to participate come **dressed in a T-shirt and shorts**. Once you arrive to the laboratory you will **read** and **sign** a BYU IRB approved consent document. Following your signature, you will be randomly assigned to 1 of 3 conditions (no saline infusion and ice application (1), saline infusion and no ice application (2), or saline infusion and ice application (3)). Once assigned you will lay on a table where an area on the side of your knee will be shaved and cleansed. Two surface thermometers will be applied. One thermometer will be applied to the front of your knee and the other will be applied to the back of your knee. If you are assigned to receive no saline infusion/ice application you will have the catheter inserted into the soft tissue outside of your knee joint while receiving the 20 minute ice application. If you are assigned to receive saline infusion, a clear plastic tube filled with 5% saline will connect a catheter inserted in the soft tissue outside of your knee joint to a 5 ml syringe filled with 5% saline. Saline infusion will last for 25 minutes with a total of 7.02 ml infused. At the 5th minute during saline infusion a 1kg ice bag will be secured to the front and back of your knee with an elastic wrap for 20 minutes. At the 20th minute, the catheter will be removed from your knee, and you will remain on the table for an additional 10 minutes. During this 10 minute period, your wound from the catheter needle will be treated with Neosporin and a band aid. Your pain will be measured using a 10 cm pain scale labeled "no pain" on the left end and "unbearable pain" on the right end. Your pain measurements will be taken before the catheter is inserted into the soft tissue outside of your knee joint, every minute during your condition, and for 10 minutes following your condition.

If you have any questions, please call or email Blaine Long at 422-9156 or blainelong@byu.edu

If you are interested, please place your name, phone # &/or email address below or on the back of this page.

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Figure B 6. Institutional Review Board Approval letter for Experiment II

INSTITUTIONAL REVIEW BOARD FOR
HUMAN SUBJECTS

November 19, 2007

Blaine C. Long
106 SFH
Campus Mail

Re: Motor Function Responses to Induced Pain and Cryotherapy

Dear Blaine,

This is to inform you that Brigham Young University's IRB has approved the above research study.

The approval period is from **11/19/2007 to 10/31/2008. Your study number is F07-0315. Please be sure to reference either this number in any correspondence with the IRB.**

Continued approval is conditional upon your compliance with the following requirements:

- A copy of the **Informed Consent Document**, approved as of **11/19/2007** is enclosed. No other consent form should be used. It must be signed by each subject prior to initiation of any protocol procedures. In addition, each subject must be given a copy of the signed consent form.
- All protocol amendments and changes to approved research must be submitted to the IRB and not be implemented until approved by the IRB.
- **The enclosed recruitment advertisement has been approved.** Advertisements, letters, Internet postings and any other media for subject recruitment must be submitted to IRB and approved prior to use.
- A few months before this date we will send out a continuing review form. There will only be two reminders. Please fill this form out in a timely manner to ensure that there is not a lapse in your approval.

If you have any questions, please do not hesitate to call me.

Sincerely,

Christopher Dromey, PhD, Chair /
Sandee M.P. Muñoz, Administrator
Institutional Review Board for Human Subjects
CD/se
Enclosure

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Figure B 7. Institutional Review Board Informed Consent to be a Research Letter for Experiment I

Consent to be a Research Subject

Title: Motor Function Responses to Induced Pain and Cryotherapy

Principal Investigator: Blaine Long, M.S., ATC (graduate student)

Faculty Advisors: Kenneth Knight PhD, ATC, Ty Hopkins PhD, ATC, Brent Feland, PhD, PT, Allen Parcel, PhD and Bruce Schaalje, PhD

Introduction and Purpose(s). This research is being conducted by Blain Long as part of his graduate research. The purposes of this study are to determine the effects of infusing a 5% saline solution into the knee and application of an ice bag (or sham ice bag) on pain and muscle activity. You have been invited to participate in this study because you meet the criteria for participation.

Procedures. You will come to the Therapeutic Modality Laboratory (123 RB) on two separate days dressed in shorts and a T-shirt. The first day will consist of a 30 minute orientation session which will include the completion of a health questionnaire and screening for a measurable muscle reflex response. If you have a measurable muscle reflex response, you will be randomly assigned to one of the following four treatment groups: 1) saline infusion/no ice bag; 2) saline infusion/ice bag; 3) saline, infusion/sham and 4) no saline infusion/no ice bag. If there is not a measurable muscle response you will not be able to participate in this study.

On the second day, you will return to the Therapeutic Modality Laboratory (123 RB) for 1 hour of testing. The knee of you dominant leg (i.e. leg with which you kick a ball) will be shaved and cleansed with a skin gel. Two electrodes will be placed in the shaved area of the knee. A third electrode will be placed over a bone on the same leg. A fourth electrode used to stimulate muscle contraction will be place over a nerve in your dominant leg. Two skin thermometers will then be applied, one on the front of the knee joint and the other on the back of the knee joint. After the placement of the electrodes and skin thermometers, you will be asked to describe any pain you feel using a pain scale. While lying on a table, you will be asked to focus your attention on a small picture on the ceiling while listening to a constant sound through headphones. A series of stimuli similar to "static electricity" will be delivered to your dominant leg in order to find a muscle response. Once a measurable response is found, 10 measurements will be taken with a 20-second rest between each measurement.

If you are assigned to receive the saline infusion/no ice bag condition, saline infusion/ice bag condition, or the saline, infusion/sham condition an area on the outside of your knee joint will be scrubbed clean with a skin cleansing wipe (povidone-iodine). A sterile catheter needle will be inserted into the cleansed area, just behind the tendon leaving a flexible catheter in your knee. A sterile plastic tube filled with 5% saline will then be connected to the catheter and to a syringe in an infusion pump. A total of 5.94 ml of 5% saline will be infused over 20 minutes. If you are assigned to receive the no saline infusion/no ice bag condition a catheter will be inserted into your knee as described above. The catheter will remain in your knee throughout the duration of the experiment but a 5% saline solution will not be infused. Depending on the group you are assigned to, an ice bag or sham ice bag will be placed on your knee. Immediately following and 30 minutes following the infusion, the muscle response and pain scale measurements will be repeated. Upon completion of the study, the catheter will be removed from your knee and the wound will be treated with antiseptic ointment (Neosporin) and a band aid.

Risks. If you receive saline infusion you will experience pain throughout the 20 minute infusion. In addition, you will continue to experience pain for approximately 15 minutes following the saline infusion. There is a slight possibility of tendon or knee joint injury when the catheter is being inserted. To minimize risk of infection at the insertion site, an area on the outside of your knee will be thoroughly cleansed with antiseptic ointment (povidone). Immediately following the study the catheter will be extracted and Neosporin and a band aid will be applied. If any adverse affects were to occur as a result of the needle stick or if the tendon or joint capsule were to become injured during catheter insertion or saline infusion, contact the investigator and you will be examined by a Licensed Board Certified Athletic Trainer or a physician.

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Figure B 7. Continued

Benefits. There are no direct benefits to you for participating in this study. Your participation in this study will help us develop a specific pain model that causes mild pain without long term affects that can be used to study the effect of pain and cold on muscle activity. Because pain is a limiting factor in many peoples lives, your participation in this study will help advance the understanding of pain and muscle activity in health care.

Confidentiality. All information about you and all data will remain confidential and will only be reported as group data with no identifying information. All data including the questionnaire will be kept secured and only the investigator involved in the study will have access to this information. Following the investigation, the questionnaires will be destroyed.

Compensation. You will receive $30.00 when you complete this study. If you do not complete this study, you will not receive any financial compensation for your participation.

Participation. Participation in this research study is voluntary. You have the right to withdraw at anytime or refuse to participate entirely without jeopardy to your class status, grade or standing with the university.

Questions about the Research:

Do you have any questions (please circle one)? YES NO

If yes, then write your question(s) on the back of this sheet and do NOT sign below until your questions have been answered satisfactorily. You may take as much time as necessary to think this over.

If you have any questions or comments regarding this study, you may contact:

Blaine Long MS, ATC, LAT
117 Richards Building
Brigham Young University
(801) 422-9156
blainelong@byu.edu

or

Kenneth L. Knight, PhD, ATC, FACSM
271 Smith Field House
Brigham Young University
(801) 422-2984
ken_knight@byu.edu

Questions about your Rights as Research Participants
If you have questions you do not feel comfortable asking the researcher, you may contact Christopher Dromey, PhD, IRB Chair, 133 TLRB, 422-6461, Christopher_dromey@byu.edu

I have read, understood, and received a copy of the above consent and desire of my own free will to participate in this study.

Signature:_____ Date:_____

Figure B 8. Research Opportunity Flyer for Experiment II

Research Subjects Needed

Male subjects between the ages of 18-30 years of age are needed for participation in a study entitled, "Motor Function Responses to Induced Pain and Cryotherapy".

You can qualify to participate in this study if you:

- are a male between the ages of 18-30
- are physically active
- have not injured either leg in the last 6 months, had surgery on either leg in the last 2 years, are free of any nerve, heart or endocrine (diabetes) conditions, and are not currently experiencing pain or consuming pain medication.

Your participation in this study will include:

- an initial screening to determine eligibility (½ hour) which includes measuring a muscle reflex response
- 1 hour of testing on a second day which includes insertion of a catheter into the knee, infusion of a saline solution, and measurement of muscle activity and pain.

If you complete the study, you will receive $30.00.

If you have any questions, please call or email Blaine Long at 422-9156 or blainelong@byu.edu

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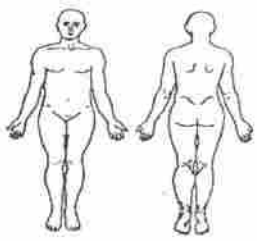
Figure B 9. McGill Pain Questionnaire and VAS for experiment II

McGill Pain Questionnaire **Subject #_____** **Pre, Post, 30 min post**

Patient's Name_____ Date_____ Time_____AM/PM

PRI: S_____ A_____ E_____ M_____ PRI (T) _____ PPI _____
(1-10) (11-15) (16) (17-20) (1-20)

1 FLICKERING QUIVERING PULSING THROBBING BEATING POUNDING	12 SICKENING SUFFOCATING	BRIEF MOMENTARY TRANSIENT	RHYTHMIC PERIODIC INTERMITTENT	CONTINUOUS STEADY CONSTANT
2 JUMPING FLASHING SHOOTING	13 FEARFUL FRIGHTFUL TERRIFYING			
3 PRICKING BORING DRILLING STABBING LANCINATING	14 PUNISHING GRUELING CRUEL VICIOUS KILLING			
4 SHARP CUTTING LACERATING	15 WRETCHED BLINDING			
5 PINCHING PRESSING GNAWING CRAMPING CRUSHING	16 ANNOYING TROUBLESOME MISERABLE INTENSE UNBEARABLE			
6 TUGGING PULLING WRENCHING	17 SPREADING RADIATING PENETRATING PIERCING			
7 HOT BURING SCALDING SEARING	18 TIGHT NUMB DRAWING SQUEEZING TEARING			
8 TINGLING ITCHY SMARTING STINGING	19 COOL COLD FREEZING			
9 DULL SORE HURTING ACHING HEAVY	20 NAGGING NAUSEATING AGONIZING DREADFUL TORTURING			
10 TENDER TAUT RASPING SPLITTING	PPI 0 NO PAIN 1 MILD PAIN 2 DISCOMFORTING 3 DISTRESSING 4 HORRIBLE 5 EXCRUCIATING	COMMENTS:		
11 TIRING EXHAUSTING				



E = EXTERNAL
I = INTERNAL

No pain Unbearable pain

Appendix C

Additional Results

Experiment I

Table C 2. Average Pain Perception Measure for Each Minute During the 3 Conditions (n = 30 subjects/condition; Mean ± SD). Measures were Taken Every Minute on a 100 mm Visual Analogue Scale

Time	Saline/cryo	No saline/cryo	Saline/sham
Pre	0.2 ± 0.4	0.3 ± 1.0	0.1 ± 0.3
1	4.8 ± 4.9	4.0 ± 3.3	2.8 ± 3.6
2	14.8 ± 12.7	3.0 ± 2.8	9.1 ± 10.5
3	28.8 ± 17.1	2.4 ± 2.2	18.6 ± 14.5
4	36.9 ± 16.9	2.4 ± 2.3	24.7 ± 19.9
5	45.9 ± 21.1	1.7 ± 1.7	31.1 ± 20.3
6	38.1 ± 17.1	7.3 ± 8.1	31.4 ± 21.6
7	41.3 ± 17.8	12.3 ± 12.	32.2 ± 22.6
8	42.1 ± 16.6	14.7 ± 13.7	30.6 ± 21.6
9	40.0 ± 19.5	12.1 ± 9.7	37.3 ± 19.2
10	40.8 ± 22.0	12.1 ± 10.3	43.2 ± 22.5
11	40.5 ± 22.4	13.0 ± 11.5	45.0 ± 22.2
12	36.0 ± 22.1	11.6 ± 10.0	46.1 ± 22.6
13	35.3 ± 21.4	11.8 ± 10.0	47.0 ± 19.3
14	36.3 ± 24.9	11.1 ± 9.0	46.0 ± 18.7
15	35.4 ± 23.6	11.9 ± 10.1	48.0 ± 17.2
16	31.4 ± 23.5	10.5 ± 8.5	46.8 ± 16.8
17	30.8 ± 23.7	10.9 ± 8.4	48.9 ± 19.3
18	34.2 ± 23.8	9.8 ± 7.0	48.9 ± 20.2
19	33.4 ± 23.7	9.3 ± 6.3	48.5 ± 21.9
20	33.5 ± 25.1	10.0 ± 7.1	49.5 ± 22.6
21	31.8 ± 24.6	10.1 ± 8.4	50.7 ± 24.5
22	26.5 ± 25.0	9.2 ± 6.8	49.2 ± 24.1
23	25.6 ± 23.4	8.2 ± 7.4	50.0 ± 24.1
24	23.9 ± 22.8	7.9 ± 6.4	50.9 ± 25.9
25	28.8 ± 23.9	7.3 ± 6.0	49.3 ± 26.7
26	25.2 ± 22.2	6.3 ± 5.9	48.3 ± 27.2
27	21.9 ± 20.6	4.6 ± 5.2	44.5 ± 26.9
28	17.7 ± 18.4	3.7 ± 3.6	41.0 ± 25.4
29	15.4 ± 15.5	1.7 ± 1.8	32.8 ± 24.1
30	8.3 ± 12.1	0.9 ± 1.6	28.1 ± 23.9
31	6.8 ± 10.5	1.1 ± 1.9	24.5 ± 22.2
32	6.3 ± 8.5	0.7 ± 1.0	22.1 ± 23.3
33	5.0 ± 6.9	0.7 ± 0.6	17.2 ± 20.9
34	4.4 ± 6.1	0.8 ± 1.0	13.9 ± 16.4
35	4.7 ± 5.9	0.7 ± 1.0	11.7 ± 16.2
Total	25.9 ± 22.6	6.8 ± 8.1	35.3 ± 24.9

Table C 3. Mixed Model Procedures for Fixed Effects Differences Between Condition and Time for Pain Perception

Effect	Numerator Degrees of Freedom	Denominator Degrees of Freedom	F-value	*P*-value
Cond	2	864	19.1	<.0001*
Time	34	864	7.4	<.0001*
Cond x Time	68	864	3.0	<.0001*

* = represents a significant difference

Table C 4. Lease Means Squares for Each Condition Across Time for Pain Perception

Effect	Time (min)	Cond	DF	t-value	*P*-value
Cond x Time	1	Saline/cryo	864	1.02	.31
Cond x Time	1	No saline/cryo	864	0.85	.40
Cond x Time	1	Saline/sham	864	0.59	.55
Cond x Time	2	Saline/cryo	864	3.13	.001*
Cond x Time	2	No saline/cryo	864	0.64	.53
Cond x Time	2	Saline/sham	864	1.93	.05
Cond x Time	3	Saline/cryo	864	6.10	<.0001*
Cond x Time	3	No saline/cryo	864	0.51	.61
Cond x Time	3	Saline/sham	864	3.94	<.0001*
Cond x Time	4	Saline/cryo	864	7.81	<.0001*
Cond x Time	4	No saline/cryo	864	0.51	.61
Cond x Time	4	Saline/sham	864	5.23	<.0001*
Cond x Time	5	Saline/cryo	864	9.72	<.0001*
Cond x Time	5	No saline/cryo	864	0.36	.72
Cond x Time	5	Saline/sham	864	6.59	<.0001*
Cond x Time	6	Saline/cryo	864	7.83	<.0001*
Cond x Time	6	No saline/cryo	864	1.50	.13
Cond x Time	6	Saline/sham	864	6.45	<.0001*
Cond x Time	7	Saline/cryo	864	8.48	<.0001*
Cond x Time	7	No saline/cryo	864	2.53	.01*
Cond x Time	7	Saline/sham	864	6.61	<.0001*
Cond x Time	8	Saline/cryo	864	8.65	<.0001*
Cond x Time	8	No saline/cryo	864	3.02	.002*
Cond x Time	8	Saline/sham	864	6.29	<.0001*
Cond x Time	9	Saline/cryo	864	8.22	<.0001*
Cond x Time	9	No saline/cryo	864	2.49	.01*
Cond x Time	9	Saline/sham	864	7.66	<.0001*
Cond x Time	10	Saline/cryo	864	8.38	<.0001*
Cond x Time	10	No saline/cryo	864	2.49	.01*
Cond x Time	10	Saline/sham	864	8.87	<.0001*
Cond x Time	11	Saline/cryo	864	8.32	<.0001*
Cond x Time	11	No saline/cryo	864	2.67	.007*
Cond x Time	11	Saline/sham	864	9.24	<.0001*
Cond x Time	12	Saline/cryo	864	7.39	<.0001*
Cond x Time	12	No saline/cryo	864	2.38	.02*
Cond x Time	12	Saline/sham	864	9.47	<.0001*
Cond x Time	13	Saline/cryo	864	7.25	<.0001*
Cond x Time	13	No saline/cryo	864	2.42	.02*
Cond x Time	13	Saline/sham	864	9.65	<.0001*

Table C 4. Continued

Cond x Time	14	Saline/cryo	864	7.46	<.0001*
Cond x Time	14	No saline/cryo	864	2.28	.02*
Cond x Time	14	Saline/sham	864	9.45	<.0001*
Cond x Time	15	Saline/cryo	864	7.27	<.0001*
Cond x Time	15	No saline/cryo	864	2.44	.01*
Cond x Time	15	Saline/sham	864	9.86	<.0001*
Cond x Time	16	Saline/cryo	864	6.45	<.0001*
Cond x Time	16	No saline/cryo	864	2.16	.03*
Cond x Time	16	Saline/sham	864	9.61	<.0001*
Cond x Time	17	Saline/cryo	864	6.33	<.0001*
Cond x Time	17	No saline/cryo	864	2.24	.03*
Cond x Time	17	Saline/sham	864	10.04	<.0001*
Cond x Time	18	Saline/cryo	864	7.03	<.0001*
Cond x Time	18	No saline/cryo	864	2.01	.04*
Cond x Time	18	Saline/sham	864	10.04	<.0001*
Cond x Time	19	Saline/cryo	864	6.86	<.0001*
Cond x Time	19	No saline/cryo	864	1.91	.06
Cond x Time	19	Saline/sham	864	9.96	<.0001*
Cond x Time	20	Saline/cryo	864	6.88	<.0001*
Cond x Time	20	No saline/cryo	864	2.05	.04*
Cond x Time	20	Saline/sham	864	10.17	<.0001*
Cond x Time	21	Saline/cryo	864	6.53	<.0001*
Cond x Time	21	No saline/cryo	864	2.07	.04*
Cond x Time	21	Saline/sham	864	10.41	<.0001*
Cond x Time	22	Saline/cryo	864	5.44	<.0001*
Cond x Time	22	No saline/cryo	864	1.89	.06
Cond x Time	22	Saline/sham	864	10.11	<.0001*
Cond x Time	23	Saline/cryo	864	5.26	<.0001*
Cond x Time	23	No saline/cryo	864	1.68	.09
Cond x Time	23	Saline/sham	864	10.27	<.0001*
Cond x Time	24	Saline/cryo	864	4.91	<.0001*
Cond x Time	24	No saline/cryo	864	1.62	.11
Cond x Time	24	Saline/sham	864	10.46	<.0001*
Cond x Time	25	Saline/cryo	864	5.92	<.0001*
Cond x Time	25	No saline/cryo	864	1.50	.13
Cond x Time	25	Saline/sham	864	10.13	<.0001*
Cond x Time	26	Saline/cryo	864	5.37	<.0001*
Cond x Time	26	No saline/cryo	864	1.34	.2
Cond x Time	26	Saline/sham	864	10.29	<.0001*
Cond x Time	27	Saline/cryo	864	4.66	<.0001*
Cond x Time	27	No saline/cryo	864	0.98	.33
Cond x Time	27	Saline/sham	864	9.48	<.0001*
Cond x Time	28	Saline/cryo	864	3.77	.0002*
Cond x Time	28	No saline/cryo	864	0.79	.43
Cond x Time	28	Saline/sham	864	8.73	<.0001*
Cond x Time	29	Saline/cryo	864	3.28	.001*
Cond x Time	29	No saline/cryo	864	0.36	.72
Cond x Time	29	Saline/sham	864	6.99	<.0001*
Cond x Time	30	Saline/cryo	864	1.77	.08
Cond x Time	30	No saline/cryo	864	0.19	.85
Cond x Time	30	Saline/sham	864	5.98	<.0001*
Cond x Time	31	Saline/cryo	864	1.45	.15

Table C 4. Continued

Cond x Time	31	No saline/cryo	864	0.23	.81
Cond x Time	31	Saline/sham	864	5.22	<.0001*
Cond x Time	32	Saline/cryo	864	1.34	.18
Cond x Time	32	No saline/cryo	864	0.15	.88
Cond x Time	32	Saline/sham	864	4.71	<.0001*
Cond x Time	33	Saline/cryo	864	1.06	.29
Cond x Time	33	No saline/cryo	864	0.15	.88
Cond x Time	33	Saline/sham	864	3.66	.0001*
Cond x Time	34	Saline/cryo	864	0.94	.35
Cond x Time	34	No saline/cryo	864	0.17	.86
Cond x Time	34	Saline/sham	864	2.96	.003*
Cond x Time	35	Saline/cryo	864	1.00	.32
Cond x Time	35	No saline/cryo	864	0.15	.88
Cond x Time	35	Saline /sham	864	2.49	.01*

* = represents a significant difference

Table C 5. Least Square Means Differences Between Condition and Time for Pain Perception

Effect	Cond	Time (min)	Cond	Time (min)	t-value	DF	*P*-value
Cond x Time	Saline/cryo	1	No saline/cryo	1	0.12	864	.90
Cond x Time	Saline/cryo	1	Saline/sham	1	0.30	864	.76
Cond x Time	No saline/cryo	1	Saline/sham	1	0.18	864	.85
Cond x Time	Saline/cryo	2	No saline/cryo	2	1.77	864	.07
Cond x Time	Saline/cryo	2	Saline/sham	2	0.85	864	.39
Cond x Time	No saline/cryo	2	Saline/sham	2	-0.91	864	.36
Cond x Time	Saline/cryo	3	No saline/cryo	3	3.95	864	.001*
Cond x Time	Saline/cryo	3	Saline/sham	3	1.53	864	.12
Cond x Time	No saline/cryo	3	Saline/sham	3	-2.43	864	.02*
Cond x Time	Saline/cryo	4	No saline/cryo	4	5.17	864	<.001*
Cond x Time	Saline/cryo	4	Saline/sham	4	1.83	864	.07
Cond x Time	No saline/cryo	4	Saline/sham	4	-3.34	864	.0009*
Cond x Time	Saline/cryo	5	No saline/cryo	5	6.62	864	<.001*
Cond x Time	Saline/cryo	5	Saline/sham	5	2.22	864	.03*
Cond x Time	No saline/cryo	5	Saline/sham	5	-4.40	864	<.001*
Cond x Time	Saline/cryo	6	No saline/cryo	6	4.47	864	<.001*
Cond x Time	Saline/cryo	6	Saline/sham	6	0.97	864	.33
Cond x Time	No saline/cryo	6	Saline/sham	6	-3.50	864	.0005*
Cond x Time	Saline/cryo	7	No saline/cryo	7	4.21	864	<.001*
Cond x Time	Saline/cryo	7	Saline/sham	7	1.32	864	.19
Cond x Time	No saline/cryo	7	Saline/sham	7	-2.89	864	.003*
Cond x Time	Saline/cryo	8	No saline/cryo	8	3.98	864	<.001*
Cond x Time	Saline/cryo	8	Saline/sham	8	1.67	864	.09
Cond x Time	No saline/cryo	8	Saline/sham	8	-2.31	864	.02*
Cond x Time	Saline/cryo	9	No saline/cryo	9	4.05	864	<.001*
Cond x Time	Saline/cryo	9	Saline/sham	9	0.39	864	.7
Cond x Time	No saline/cryo	9	Saline/sham	9	-3.66	864	.0003*
Cond x Time	Saline/cryo	10	No saline/cryo	10	4.17	864	<.001*
Cond x Time	Saline/cryo	10	Saline/sham	10	-0.35	864	.72
Cond x Time	No saline/cryo	10	Saline/sham	10	-4.52	864	.025*
Cond x Time	Saline/cryo	11	No saline/cryo	11	3.99	864	<.001*
Cond x Time	Saline/cryo	11	Saline/sham	11	-0.65	864	.51
Cond x Time	No saline/cryo	11	Saline/sham	11	-4.65	864	.01*
Cond x Time	Saline/cryo	12	No saline/cryo	12	3.54	864	.0004*
Cond x Time	Saline/cryo	12	Saline/sham	12	-1.47	864	.14
Cond x Time	No saline/cryo	12	Saline/sham	12	-5.01	864	.002*
Cond x Time	Saline/cryo	13	No saline/cryo	13	3.41	864	.0007*
Cond x Time	Saline/cryo	13	Saline/sham	13	-1.70	864	.09
Cond x Time	No saline/cryo	13	Saline/sham	13	-5.11	864	<.001*
Cond x Time	Saline/cryo	14	No saline/cryo	14	3.66	864	.0003*
Cond x Time	Saline/cryo	14	Saline/sham	14	-1.41	864	.16
Cond x Time	No saline/cryo	14	Saline/sham	14	-5.07	864	.002*
Cond x Time	Saline/cryo	15	No saline/cryo	15	3.41	864	.0007*
Cond x Time	Saline/cryo	15	Saline/sham	15	-1.83	864	.07
Cond x Time	No saline/cryo	15	Saline/sham	15	-5.24	864	.0009*
Cond x Time	Saline/cryo	16	No saline/cryo	16	3.04	864	.002*
Cond x Time	Saline/cryo	16	Saline/sham	16	-2.24	864	.025*
Cond x Time	No saline/cryo	16	Saline/sham	16	-5.27	864	.0008*
Cond x Time	Saline/cryo	17	No saline/cryo	17	2.89	864	.003*

Table C 5. Continued

Cond x Time	Saline/cryo	17	Saline/sham	17	-2.63	864	.008*
Cond x Time	No saline/cryo	17	Saline/sham	17	-5.52	864	.0002*
Cond x Time	Saline/cryo	18	No saline/cryo	18	3.54	864	.0004*
Cond x Time	Saline/cryo	18	Saline/sham	18	-2.14	864	.033*
Cond x Time	No saline/cryo	18	Saline/sham	18	-5.68	864	<.001*
Cond x Time	Saline/cryo	19	No saline/cryo	19	3.50	864	.0005*
Cond x Time	Saline/cryo	19	Saline/sham	19	-2.19	864	.028*
Cond x Time	No saline/cryo	19	Saline/sham	19	-5.69	864	<.001*
Cond x Time	Saline/cryo	20	No saline/cryo	20	3.41	864	.0007*
Cond x Time	Saline /cryo	20	Saline/sham	20	-2.32	864	.02*
Cond x Time	No saline /cryo	20	Saline/sham	20	-5.74	864	<.001*
Cond x Time	Saline/cryo	21	No saline/cryo	21	3.15	864	.001*
Cond x Time	Saline/cryo	21	Saline/sham	21	-2.75	864	.006*
Cond x Time	No saline/cryo	21	Saline/sham	21	-5.90	864	<.001*
Cond x Time	Saline/cryo	22	No saline/cryo	22	2.51	864	.012*
Cond x Time	Saline/cryo	22	Saline/sham	22	-3.30	864	<.0001*
Cond x Time	No saline/cryo	22	Saline/sham	22	-5.81	864	<.0001*
Cond x Time	Saline/cryo	23	No saline/cryo	23	2.53	864	<.0001*
Cond x Time	Saline/cryo	23	Saline/sham	23	-3.54	864	.0004*
Cond x Time	No saline/cryo	23	Saline/sham	23	-6.07	864	<.0001*
Cond x Time	Saline/cryo	24	No saline/cryo	24	2.32	864	.002*
Cond x Time	Saline cryo	24	Saline/sham	24	-3.92	864	<.000*
Cond x Time	No saline/cryo	24	Saline/sham	24	-6.25	864	<.0001*
Cond x Time	Saline/cryo	25	No saline/cryo	25	3.12	864	.0001*
Cond x Time	Saline/cryo	25	Saline/sham	25	-2.98	864	.0003*
Cond x Time	No saline/cryo	25	Saline/sham	25	-6.10	864	<.0001*
Cond x Time	Saline/cryo	26	No saline/cryo	26	2.85	864	.004*
Cond x Time	Saline/cryo	26	Saline/sham	26	-3.48	864	.0005*
Cond x Time	No saline/cryo	26	Saline/sham	26	-6.32	864	<.001*
Cond x Time	Saline/cryo	27	No saline/cryo	27	2.61	864	.009*
Cond x Time	Saline/cryo	27	Saline/sham	27	-3.40	864	.0007*
Cond x Time	No saline/cryo	27	Saline/sham	27	-6.01	864	<.0001*
Cond x Time	Saline/cryo	28	No saline/cryo	28	2.11	864	.04*
Cond x Time	Saline/cryo	28	Saline/sham	28	-3.51	864	.0005*
Cond x Time	No saline/cryo	28	Saline/sham	28	-5.62	864	.0001*
Cond x Time	Saline/cryo	29	No saline/cryo	29	2.06	864	.04*
Cond x Time	Saline/cryo	29	Saline/sham	29	-2.62	864	.008*
Cond x Time	No saline/cryo	29	Saline/sham	29	-4.68	864	.01*
Cond x Time	Saline /cryo	30	No saline/cryo	30	1.11	864	.27
Cond x Time	Saline/cryo	30	Saline/sham	30	-2.98	864	.002*
Cond x Time	No saline/cryo	30	Saline/sham	30	-4.10	864	<.0001*
Cond x Time	Saline/cryo	31	No saline/cryo	31	0.86	864	.39
Cond x Time	Saline/cryo	31	Saline/sham	31	-2.67	864	.007*
Cond x Time	No saline/cryo	31	Saline/sham	31	-3.52	864	.0004*
Cond x Time	Saline/cryo	32	No saline/cryo	32	0.84	864	.4
Cond x Time	Saline/cryo	32	Saline/sham	32	-2.38	864	.02*
Cond x Time	No saline/cryo	32	Saline/sham	32	-3.22	864	.001*
Cond x Time	Saline/cryo	33	No saline/cryo	33	0.65	864	.52
Cond x Time	Saline/cryo	33	Saline/sham	33	-1.84	864	.07
Cond x Time	No saline/cryo	33	Saline/sham	33	-2.48	864	.01*
Cond x Time	Saline/cryo	34	No saline/cryo	34	0.54	864	.6
Cond x Time	Saline/cryo	34	Saline/sham	34	-1.43	864	.15

Table C 5. Continued

Cond x Time	No saline/cryo	34	Saline/sham	34	-1.97	864	.04*
Cond x Time	Saline/cryo	35	No saline/cryo	35	0.60	864	.55
Cond x Time	Saline/cryo	35	Saline/sham	35	-1.05	864	.29
Cond x Time	No saline/cryo	35	Saline/sham	35	-1.66	864	.09

* = represents a significant difference

Table C 6. Sequential Time Differences for Pain Perception Within Each Condition

Effect	Cond	Time (min)	Time (min)	t-value	DF	*P*-value
Cond x Time	Saline/cryo	1	2	-5.7	864	<.0001*
Cond x Time	Saline/cryo	2	3	-8.0	864	<.0001*
Cond x Time	Saline/cryo	3	4	-4.6	864	.02*
Cond x Time	Saline /cryo	4	5	-5.1	864	.001*
Cond x Time	Saline/cryo	5	6	3.5	864	.0005*
Cond x Time	Saline/cryo	6	7	-1.8	864	.07
Cond x Time	Saline/cryo	7	8	-0.4	864	.65
Cond x Time	Saline/cryo	8	9	1.2	864	.23
Cond x Time	Saline/cryo	9	10	-0.46	864	.65
Cond x Time	Saline/cryo	10	11	0.17	864	.86
Cond x Time	Saline/cryo	11	12	2.56	864	.01*
Cond x Time	Saline /cryo	12	13	0.40	864	.69
Cond x Time	Saline /cryo	13	14	-0.57	864	.57
Cond x Time	Saline /cryo	14	15	0.51	864	.61
Cond x Time	Saline/cryo	15	16	2.28	864	.02*
Cond x Time	Saline/cryo	16	17	0.34	864	.73
Cond x Time	Saline/cryo	17	18	-1.94	864	.04*
Cond x Time	Saline/cryo	18	19	0.46	864	.65
Cond x Time	Saline/cryo	19	20	-0.06	864	.95
Cond x Time	Saline/cryo	20	21	0.97	864	.33
Cond x Time	Saline/cryo	21	22	3.02	864	.002*
Cond x Time	Saline/cryo	22	23	0.51	864	.61
Cond x Time	Saline/cryo	23	24	0.97	864	.33
Cond x Time	Saline/cryo	24	25	-2.79	864	.005*
Cond x Time	Saline/cryo	25	26	1.65	864	.09
Cond x Time	Saline/cryo	26	27	1.88	864	.06*
Cond x Time	Saline/cryo	27	28	2.39	864	.02*
Cond x Time	Saline/cryo	28	29	1.31	864	.19
Cond x Time	Saline/cryo	29	30	4.04	864	<.0001*
Cond x Time	Saline/cryo	30	31	0.85	864	.39
Cond x Time	Saline/cryo	31	32	0.28	864	.78
Cond x Time	Saline/cryo	32	33	0.74	864	.46
Cond x Time	Saline/cryo	33	34	0.34	864	.73
Cond x Time	Saline/cryo	34	35	-0.17	864	.86
Cond x Time	No saline/cryo	1	2	0.57	864	.57
Cond x Time	No saline/cryo	2	3	0.34	864	.73
Cond x Time	No saline/cryo	3	4	0.001	864	1.00
Cond x Time	No saline/cryo	4	5	0.40	864	.69
Cond x Time	No saline/cryo	5	6	-2.51	864	.012*
Cond x Time	No saline/cryo	6	7	-2.85	864	.004*
Cond x Time	No saline/cryo	7	8	-1.37	864	.17
Cond x Time	No saline/cryo	8	9	1.48	864	.14
Cond x Time	No saline/cryo	9	10	0.00	864	1.00
Cond x Time	No saline/cryo	10	11	-0.51	864	.61
Cond x Time	No saline/cryo	11	12	0.80	864	.42
Cond x Time	No saline/cryo	12	13	-0.11	864	.91
Cond x Time	No saline/cryo	13	14	0.40	864	.69
Cond x Time	No saline/cryo	14	15	-0.46	864	.65
Cond x Time	No saline/cryo	15	16	0.80	864	.42
Cond x Time	No saline/cryo	16	17	-0.23	864	.82

Table C 6. Continued

Cond x Time	No saline/cryo	17	18	0.63	864	.53
Cond x Time	No saline/cryo	18	19	0.28	864	.78
Cond x Time	No saline/cryo	19	20	-0.40	864	.69
Cond x Time	No saline/cryo	20	21	-0.06	864	.95
Cond x Time	No saline/cryo	21	22	0.51	864	.61
Cond x Time	No saline/cryo	22	23	0.57	864	.57
Cond x Time	No saline/cryo	23	24	0.17	864	.86
Cond x Time	No saline/cryo	24	25	0.34	864	.73
Cond x Time	No saline/cryo	25	26	0.46	864	.65
Cond x Time	No saline/cryo	26	27	0.97	864	.33
Cond x Time	No saline/cryo	27	28	0.51	864	.61
Cond x Time	No saline/cryo	28	29	1.14	864	.26
Cond x Time	No saline/cryo	29	30	0.46	864	.65
Cond x Time	No saline/cryo	30	31	-0.11	864	.91
Cond x Time	No saline/cryo	31	32	0.23	864	.82
Cond x Time	No saline/cryo	32	33	0.00	864	1.00
Cond x Time	No saline/cryo	33	34	-0.06	864	.95
Cond x Time	No saline/cryo	34	35	0.06	864	.95
Cond x Time	Saline/sham	1	2	-3.59	864	.0004*
Cond x Time	Saline/sham	2	3	-5.41	864	<.0001*
Cond x Time	Saline/sham	3	4	-3.47	864	.0005*
Cond x Time	Saline/sham	4	5	-3.64	864	.0003*
Cond x Time	Saline/sham	5	6	-0.13	864	.89
Cond x Time	Saline/sham	6	7	-0.46	864	.65
Cond x Time	Saline/sham	7	8	0.91	864	.36
Cond x Time	Saline/sham	8	9	-3.81	864	.0001*
Cond x Time	Saline/sham	9	10	-3.36	864	.0008*
Cond x Time	Saline/sham	10	11	-1.02	864	.31
Cond x Time	Saline/sham	11	12	-0.63	864	.53
Cond x Time	Saline/sham	12	13	-0.51	864	.61
Cond x Time	Saline/sham	13	14	0.57	864	.57
Cond x Time	Saline/sham	14	15	-1.14	864	.26
Cond x Time	Saline/sham	15	16	0.68	864	.49
Cond x Time	Saline/sham	16	17	-1.20	864	.23
Cond x Time	Saline/sham	17	18	0.00	864	1.00
Cond x Time	Saline/sham	18	19	0.23	864	.82
Cond x Time	Saline/sham	19	20	-0.57	864	.57
Cond x Time	Saline/sham	20	21	-0.68	864	.49
Cond x Time	Saline/sham	21	22	0.85	864	.39
Cond x Time	Saline/sham	22	23	-0.46	864	.65
Cond x Time	Saline/sham	23	24	-0.51	864	.61
Cond x Time	Saline/sham	24	25	0.91	864	.36
Cond x Time	Saline/sham	25	26	0.46	864	.65
Cond x Time	Saline/sham	26	27	2.16	864	.03*
Cond x Time	Saline/sham	27	28	1.99	864	.04*
Cond x Time	Saline/sham	28	29	4.67	864	<.0001*
Cond x Time	Saline/sham	30	31	2.05	864	.04*
Cond x Time	Saline/sham	31	32	1.37	864	.17
Cond x Time	Saline/sham	32	33	2.79	864	.005*
Cond x Time	Saline/sham	33	34	1.88	864	.06*
Cond x Time	Saline/sham	34	35	1.25	864	.21

* = represents a significant difference

Table C 7. Average Patella Surface Temperature During Each Phase for Each of the 3 Conditions (n = 30 Subjects/Condition; Mean ± SD)

Phase	Saline/cryo[*]	No saline/cryo[†]	Saline/sham
Preapplication	28.3 ± 1.1	27.7 ± 1.6	28.0 ± 1.2
Application[‡]	7.2 ± 4.5	6.7 ± 4.2	28.2 ± 1.1
Postapplication[§]	11.0 ± 2.3	11.5 ±2.4	28.3 ± 1.5

[*]Application < postapplication & preapplication. Postapplication < preapplication
[†]Application < postapplication & preapplication. Postapplication < preapplication
[‡]Saline/cryo & no saline/cryo < saline/sham
[§]Saline/cryo & no saline/cryo < saline/sham

Table C 8. Mixed Procedures for Fixed Effects Differences Between Condition and Application Phase for Patella Surface Temperature

Effect	Numerator Degrees of Freedom	Denominator Degrees of Freedom	F-value	*P*-value
Cond	2	945	587.4	<.0001[*]
Phase	2	945	1780.3	<.0001[*]
Cond x Phase	4	945	456.5	<.0001[*]
Cond x Time (Phase)	99	945	25.8	<.0001[*]

[*] = represents a significant difference

Table C 9. Differences of Least Means Squares Between Condition and Application Phase for Patella Surface Temperature (°C)

Effect	Cond	Phase	Cond	Phase	t-value	DF	*P*-value
Cond x Phase	Saline/cryo	Preappl	Saline/cryo	Appl	51.8	945	<.0001*
Cond x Phase	Saline/cryo	Preappl	Saline/cryo	Postappl	32.9	945	<.0001*
Cond x Phase	Saline/cryo	Preappl	No saline/cryo	Preappl	1.0	945	.32
Cond x Phase	Saline/cryo	Preappl	No saline/cryo	Appl	37.9	945	<.0001*
Cond x Phase	Saline/cryo	Preappl	No saline/cryo	Postappl	27.8	945	<.0001*
Cond x Phase	Saline/cryo	Preappl	Saline/sham	Preappl	0.5	945	.63
Cond x Phase	Saline/cryo	Preappl	Saline/sham	Appl	0.2	945	.82
Cond x Phase	Saline/cryo	Preappl	Saline/sham	Postappl	0.05	945	.96
Cond x Phase	Saline/cryo	Appl	Saline/cryo	Postappl	-9.5	945	<.0001*
Cond x Phase	Saline/cryo	Appl	No saline/cryo	Preappl	-35.9	945	<.0001*
Cond x Phase	Saline/cryo	Appl	No saline/cryo	Appl	1.1	945	.29
Cond x Phase	Saline/cryo	Appl	No saline/cryo	Postappl	-7.8	945	<.0001*
Cond x Phase	Saline/cryo	Appl	Saline/sham	Preappl	-36.4	945	<.0001*
Cond x Phase	Saline/cryo	Appl	Saline/sham	Appl	-41.03	945	<.0001*
Cond x Phase	Saline/cryo	Appl	Saline/sham	Postappl	-38.4	945	<.0001*
Cond x Phase	Saline/cryo	Postappl	No saline/cryo	Preappl	-27.7	945	<.0001*
Cond x Phase	Saline/cryo	Postappl	No saline/cryo	Appl	7.8	945	<.0001*
Cond x Phase	Saline/cryo	Postappl	No saline/cryo	Postappl	-1.0	945	.36
Cond x Phase	Saline/cryo	Postappl	Saline/sham	Preappl	-28.2	945	<.0001*
Cond x Phase	Saline/cryo	Postappl	Saline/sham	Appl	-31.4	945	<.0001*
Cond x Phase	Saline/cryo	Postappl	Saline/sham	Postappl	-29.7	945	<.0001*
Cond x Phase	No saline/cryo	Preappl	No saline/cryo	Appl	51.7	945	<.0001*
Cond x Phase	No saline/cryo	Preappl	No saline/cryo	Postappl	30.7	945	<.0001*
Cond x Phase	No saline/cryo	Preappl	Saline/sham	Preappl	-0.5	945	.62
Cond x Phase	No saline/cryo	Preappl	Saline/sham	Appl	-0.9	945	.40
Cond x Phase	No saline/cryo	Preappl	Saline/sham	Postappl	-1.0	945	.33
Cond x Phase	No saline/cryo	Appl	No saline/cryo	Postappl	-12.2	945	<.0001*
Cond x Phase	No saline/cryo	Appl	Saline/sham	Preappl	-37.4	945	<.0001*
Cond x Phase	No saline/cryo	Appl	Saline/sham	Appl	-42.1	945	<.0001*
Cond x Phase	No saline/cryo	Appl	Saline/sham	Postappl	-39.4	945	<.0001*
Cond x Phase	No saline/cryo	Postappl	Saline/sham	Preappl	-27.3	945	<.0001*
Cond x Phase	No saline/cryo	Postappl	Saline/sham	Appl	-30.4	945	<.0001*
Cond x Phase	No saline/cryo	Postappl	Saline/sham	Postappl	-28.8	945	<.0001*
Cond x Phase	Saline/sham	Preappl	Saline/sham	Appl	-0.4	945	.67
Cond x Phase	Saline/sham	Preappl	Saline/sham	Postappl	-0.5	945	.60
Cond x Phase	Saline/sham	Appl	Saline/sham	Postappl	-0.3	945	.80

* = represents a significant difference

Table C 10. Average Popliteal Surface Temperature During Each Phase for Each of the 3 Conditions (n = 30 Subjects/Condition; Mean ± SD)

Phase	Saline/cryo*	No saline/cryo†	Saline/sham
Preapplication	32.81± 0.68	31.68 ± 1.92	32.58 ± 1.15
Application‡	8.35 ± 4.59	7.39 ± 4.22	32.43 ± 1.32
Postapplication§	17.67 ± 3.85	18.47 ± 4.25	33.04 ± 1.26§

*Application < postapplication & preapplication. Postapplication < preapplication
†Application < postapplication & preapplication. Postapplication < preapplication
‡Saline/cryo & no saline/cryo < saline/sham
§Saline/cryo & no saline/cryo < saline/sham

Table C 11. Mixed Procedures for Fixed Effects Differences Between Condition and Application Phase for Popliteal Surface Temperature (°C)

Effect	Numerator Degrees of Freedom	Denominator Degrees of Freedom	F-value	*P*-value
Cond	2	945	478.6	<.0001*
Phase	2	945	2161.5	<.0001*
Cond x Phase	4	945	523.4	<.0001*
Cond x Time (Phase)	99	945	32.5	<.0001*

* = represents a significant difference

Table C 12. Differences of Least Means Squares Between Condition and Application Phase for Popliteal Surface Temperature (°C)

Effect	Cond	Phase	Cond	Phase	t-value	DF	*P*-value
Cond x Phase	Saline/cryo	Preappl	Saline/cryo	Appl	54.9	945	<.0001*
Cond x Phase	Saline/cryo	Preappl	Saline/cryo	Postappl	27.01	945	<.0001*
Cond x Phase	Saline/cryo	Preappl	No saline/cryo	Preappl	1.6	945	.106
Cond x Phase	Saline/cryo	Preappl	No saline/cryo	Appl	39.6	945	<.0001*
Cond x Phase	Saline/cryo	Preappl	No saline/cryo	Postappl	21.1	945	<.0001*
Cond x Phase	Saline/cryo	Preappl	Saline/sham	Preappl	0.3	945	.74
Cond x Phase	Saline/cryo	Preappl	Saline/sham	Appl	0.6	945	.55
Cond x Phase	Saline/cryo	Preappl	Saline/sham	Postappl	-0.3	945	.74
Cond x Phase	Saline/cryo	Appl	Saline/cryo	Postappl	-21.8	945	<.0001*
Cond x Phase	Saline/cryo	Appl	No saline/cryo	Preappl	-36.3	945	<.0001*
Cond x Phase	Saline/cryo	Appl	No saline/cryo	Appl	1.7	945	.098
Cond x Phase	Saline/cryo	Appl	No saline/cryo	Postappl	-16.4	945	<.0001*
Cond x Phase	Saline/cryo	Appl	Saline/sham	Preappl	-37.7	945	<.0001*
Cond x Phase	Saline/cryo	Appl	Saline/sham	Appl	-41.8	945	<.0001*
Cond x Phase	Saline/cryo	Appl	Saline/sham	Postappl	-40.05	945	<.0001*
Cond x Phase	Saline/cryo	Postappl	No saline/cryo	Preappl	-20.6	945	<.0001*
Cond x Phase	Saline/cryo	Postappl	No saline/cryo	Appl	16.7	945	<.0001*
Cond x Phase	Saline/cryo	Postappl	No saline/cryo	Postappl	-1.2	945	.22
Cond x Phase	Saline/cryo	Postappl	Saline/sham	Preappl	-21.9	945	<.0001*
Cond x Phase	Saline/cryo	Postappl	Saline/sham	Appl	-23.9	945	<.0001*
Cond x Phase	Saline/cryo	Postappl	Saline/sham	Postappl	-23.5	945	<.0001*
Cond x Phase	No saline/cryo	Preappl	No saline/cryo	Appl	54.5	945	<.0001*
Cond x Phase	No saline/cryo	Preappl	No saline/cryo	Postappl	23.6	945	<.0001*
Cond x Phase	No saline/cryo	Preappl	Saline/sham	Preappl	-1.3	945	.19
Cond x Phase	No saline/cryo	Preappl	Saline/sham	Appl	-1.2	945	.24
Cond x Phase	No saline/cryo	Preappl	Saline/sham	Postappl	-2.01	945	.04
Cond x Phase	No saline/cryo	Appl	No saline/cryo	Postappl	-25.9	945	<.0001*
Cond x Phase	No saline/cryo	Appl	Saline/sham	Preappl	-39.2	945	<.0001*
Cond x Phase	No saline/cryo	Appl	Saline/sham	Appl	-43.4	945	<.0001*
Cond x Phase	No saline/cryo	Appl	Saline/sham	Postappl	-41.6	945	<.0001*
Cond x Phase	No saline/cryo	Postappl	Saline/sham	Preappl	-20.8	945	<.0001*
Cond x Phase	No saline/cryo	Postappl	Saline/sham	Appl	-22.6	945	<.0001*
Cond x Phase	No saline/cryo	Postappl	Saline/sham	Postappl	-22.3	945	<.0001*
Cond x Phase	Saline/sham	Preappl	Saline/sham	Appl	0.4	945	.73
Cond x Phase	Saline/sham	Preappl	Saline/sham	Postappl	-0.8	945	.41
Cond x Phase	Saline/sham	Appl	Saline/sham	Postappl	-1.4	945	.15

* = represents a significant difference

Table C 13. Average Ambient Temperature During Each Phase for Each of the 3 Conditions (n = 30 Subjects/Condition; Mean ± SD)

Phase	Saline/cryo	No saline/cryo	Saline/sham
Preapplication	21.6 ± 0.2	21.7 ± 0.2	21.7 ± 0.5
Application	21.6 ± 0.2	21.7 ± 0.3	21.8 ± 0.2
Postapplication	21.7 ± 0.2	21.7 ± 0.3	21.8 ± 0.2

Table C 14. All Data for Each Subjected Stacked

Sub	Cond	Time	Phase	VAS	Pain Reported	Pat. (°C)	Pop. (°C)	Amb. (°C)
1	3	0	0	0		27.30	34.87	21.99
1	3	1	0	1	5	27.33	34.89	21.92
1	3	2	0	9	5	26.99	35.02	21.90
1	3	3	0	24	5	27.19	35.02	21.98
1	3	4	0	49	5	27.08	35.06	21.96
1	3	5	0	58	5	27.01	35.09	18.19
1	3	6	1	60	4	26.90	35.10	22.03
1	3	7	1	59	4	26.66	34.33	22.00
1	3	8	1	48	3	26.63	34.91	22.00
1	3	9	1	55	5	26.59	35.23	21.90
1	3	10	1	62	5	26.68	35.37	21.98
1	3	11	1	62	4	26.72	35.45	22.04
1	3	12	1	64	5	26.72	35.54	21.98
1	3	13	1	64	4	26.77	35.59	22.04
1	3	14	1	61	4	26.81	35.64	21.96
1	3	15	1	66	4	26.85	35.68	22.05
1	3	16	1	69	5	26.89	35.72	21.98
1	3	17	1	68	4	26.93	35.73	22.09
1	3	18	1	68	5	26.94	35.77	21.94
1	3	19	1	69	5	26.97	35.79	21.96
1	3	20	1	68	3	27.01	35.85	21.92
1	3	21	1	78	5	27.04	35.85	22.04
1	3	22	1	74	4	27.08	35.88	21.96
1	3	23	1	74	4	27.10	35.90	21.95
1	3	24	1	79	4	27.13	35.95	21.99
1	3	25	1	75	4	26.83	35.82	21.92
1	3	26	2	64	3	26.30	35.61	21.95
1	3	27	2	44	3	26.45	35.86	22.03
1	3	28	2	40	3	26.50	36.01	22.14
1	3	29	2	35	3	26.54	36.09	22.13
1	3	30	2	30	3	26.63	36.16	22.09
1	3	31	2	20	4	26.66	36.22	22.08
1	3	32	2	23	4	26.59	36.24	22.07
1	3	33	2	25	3	26.63	36.26	22.09
1	3	34	2	22	3	26.62	36.29	22.07
1	3	35	2	16	3	26.65	36.27	22.08
2	2	0	0	0		27.02	30.67	21.78
2	2	1	0	0	4	26.93	30.94	21.74

Table C 14. Continued

2	2	2	0	2	4	27.62	31.05	22.32
2	2	3	0	2	4	27.15	31.99	21.92
2	2	4	0	2	4	27.29	32.36	21.74
2	2	5	0	2	4	27.35	32.26	21.65
2	2	6	1	2	4	18.68	31.75	21.83
2	2	7	1	2	4	15.12	20.04	21.95
2	2	8	1	2	4	10.17	13.36	22.04
2	2	9	1	1	4	7.20	8.76	21.96
2	2	10	1	1	4	6.35	7.77	21.96
2	2	11	1	1	4	5.74	7.23	21.95
2	2	12	1	2	4	5.09	6.89	21.92
2	2	13	1	2	4	4.53	6.58	21.96
2	2	14	1	1	4	4.12	6.22	22.01
2	2	15	1	1	4	3.86	6.00	22.00
2	2	16	1	1	4	3.61	5.87	21.95
2	2	17	1	2	4	3.42	5.78	21.91
2	2	18	1	2	4	3.25	5.64	21.85
2	2	19	1	2	4	3.15	5.54	22.04
2	2	20	1	2	4	2.97	5.38	21.92
2	2	21	1	2	4	2.84	5.19	21.96
2	2	22	1	3	4	2.69	5.07	21.91
2	2	23	1	2	4	2.54	4.97	21.94
2	2	24	1	2	4	2.61	5.14	22.00
2	2	25	1	2	4	6.10	10.60	21.99
2	2	26	2	1	4	7.74	13.65	22.01
2	2	27	2	2	4	8.89	15.73	21.82
2	2	28	2	2	4	9.57	17.40	21.91
2	2	29	2	2	4	10.49	18.95	22.01
2	2	30	2	2	4	11.29	20.25	21.87
2	2	31	2	2	4	12.18	21.36	21.95
2	2	32	2	1	4	13.36	22.19	21.98
2	2	33	2	1	4	14.42	22.82	21.94
2	2	34	2	2	4	15.30	23.42	21.91
2	2	35	2	1	4	15.95	23.85	21.89
3	3	0	0	0	4	26.84	32.23	21.65
3	3	1	0	0	5	25.45	32.26	21.86
3	3	2	0	4	5	25.28	32.27	21.76
3	3	3	0	7	5	25.31	32.31	21.94
3	3	4	0	3	5	25.20	32.32	21.74
3	3	5	0	17	5	25.10	32.44	21.82
3	3	6	1	19	4	26.63	31.70	21.72
3	3	7	1	23	5	26.67	31.55	21.90
3	3	8	1	35	5	26.74	31.39	21.77
3	3	9	1	43	5	26.77	31.37	21.92
3	3	10	1	52	5	26.77	31.37	21.89
3	3	11	1	53	4	26.81	31.42	21.82
3	3	12	1	60	5	26.80	31.47	21.98
3	3	13	1	59	5	26.81	31.55	21.92
3	3	14	1	55	4	26.83	31.62	21.81

Table C 14. Continued

3	3	15	1	59	4	26.83	31.71	21.95
3	3	16	1	60	5	26.88	31.81	21.78
3	3	17	1	68	5	26.90	31.91	21.85
3	3	18	1	73	5	26.92	31.96	21.78
3	3	19	1	79	5	26.95	32.06	21.99
3	3	20	1	83	4	26.94	32.11	21.89
3	3	21	1	89	5	26.95	32.19	21.83
3	3	22	1	88	4	26.99	32.29	21.96
3	3	23	1	92	4	27.01	32.35	21.82
3	3	24	1	95	5	27.04	32.42	21.91
3	3	25	1	97	5	27.04	32.47	21.81
3	3	26	2	95	4	26.57	32.09	21.89
3	3	27	2	90	3	26.50	32.17	21.85
3	3	28	2	85	3	26.49	32.24	21.89
3	3	29	2	86	4	26.47	32.33	22.04
3	3	30	2	81	3	26.48	32.45	22.01
3	3	31	2	76	3	26.40	32.49	21.94
3	3	32	2	79	4	26.44	32.55	21.95
3	3	33	2	68	3	26.45	32.63	21.92
3	3	34	2	54	3	26.43	32.69	21.91
3	3	35	2	54	3	26.41	32.74	21.92
4	1	0	0	1		28.30	32.38	21.67
4	1	1	0	5	5	28.30	32.38	21.67
4	1	2	0	11	5	28.26	32.68	21.60
4	1	3	0	23	5	28.26	32.73	21.64
4	1	4	0	35	4	28.21	32.76	21.65
4	1	5	0	47	5	28.23	32.92	21.65
4	1	6	1	44	3	23.25	23.07	21.71
4	1	7	1	52	5	15.62	12.54	21.82
4	1	8	1	53	3	12.28	9.69	21.65
4	1	9	1	59	5	9.85	8.13	21.72
4	1	10	1	43	3	8.28	7.03	21.91
4	1	11	1	39	3	7.14	6.41	21.62
4	1	12	1	42	4	6.61	5.30	21.65
4	1	13	1	53	4	5.76	5.84	21.69
4	1	14	1	51	5	5.20	5.77	21.71
4	1	15	1	53	4	4.73	5.66	21.67
4	1	16	1	45	3	4.40	5.39	21.73
4	1	17	1	33	3	4.11	5.20	21.73
4	1	18	1	34	3	3.97	5.05	21.69
4	1	19	1	42	5	3.82	5.04	21.74
4	1	20	1	45	4	3.54	4.89	21.64
4	1	21	1	45	4	3.43	4.81	21.63
4	1	22	1	43	4	3.21	4.70	21.74
4	1	23	1	33	3	3.08	4.72	21.73
4	1	24	1	33	3	3.09	4.78	21.67
4	1	25	1	35	3	2.82	4.55	21.73
4	1	26	2	40	5	6.10	9.77	21.62
4	1	27	2	41	4	7.20	12.96	21.82

Table C 14. Continued

4	1	28	2	38	4	7.89	15.78	21.58
4	1	29	2	34	3	8.74	18.13	21.65
4	1	30	2	21	3	9.45	19.66	21.72
4	1	31	2	15	3	10.06	20.59	21.77
4	1	32	2	12	3	10.69	21.37	21.46
4	1	33	2	11	4	11.33	21.80	21.73
4	1	34	2	13	3	11.91	22.31	21.80
4	1	35	2	8	3	12.44	22.87	21.74
5	2	0	0	0	4	25.78	31.11	21.44
5	2	1	0	0	4	25.61	31.18	21.46
5	2	2	0	0	4	26.02	31.47	21.32
5	2	3	0	0	4	25.83	31.39	21.44
5	2	4	0	0	4	25.85	31.62	21.41
5	2	5	0	0	4	25.61	31.62	21.54
5	2	6	1	2	5	17.23	23.43	21.32
5	2	7	1	2	4	12.06	18.71	21.08
5	2	8	1	3	4	10.37	16.23	21.42
5	2	9	1	3	4	9.76	14.78	21.35
5	2	10	1	4	4	8.99	13.73	21.36
5	2	11	1	4	4	7.62	13.04	21.44
5	2	12	1	4	4	7.23	12.54	21.41
5	2	13	1	4	4	6.47	11.95	21.41
5	2	14	1	5	4	6.99	12.32	21.33
5	2	15	1	4	4	5.51	10.94	21.42
5	2	16	1	4	4	5.14	10.40	21.42
5	2	17	1	4	4	4.84	10.25	21.44
5	2	18	1	4	4	4.84	9.99	21.18
5	2	19	1	5	4	4.53	9.68	21.51
5	2	20	1	5	4	4.34	9.60	21.45
5	2	21	1	3	4	4.00	9.51	21.60
5	2	22	1	4	4	3.78	9.38	21.47
5	2	23	1	5	4	3.55	9.40	21.55
5	2	24	1	4	4	3.25	9.05	21.56
5	2	25	1	4	4	2.82	6.68	21.54
5	2	26	2	4	4	7.24	13.00	21.41
5	2	27	2	5	4	9.39	15.83	21.37
5	2	28	2	5	4	9.57	16.44	21.46
5	2	29	2	0	3	10.22	17.67	21.20
5	2	30	2	1	4	10.76	17.90	21.85
5	2	31	2	1	4	11.41	19.14	22.39
5	2	32	2	1	4	11.98	20.42	21.42
5	2	33	2	1	4	12.32	21.06	21.24
5	2	34	2	1	4	12.90	21.96	21.56
5	2	35	2	1	4	13.12	22.19	21.50
6	3	0	0	1		29.45	31.70	21.37
6	3	1	0	10	5	29.50	31.84	21.24
6	3	2	0	12	4	29.36	32.00	21.46
6	3	3	0	21	5	29.42	32.10	21.19
6	3	4	0	25	4	29.50	32.32	21.51

Table C 14. Continued

6	3	5	0	26	4	29.38	32.37	21.28
6	3	6	1	24	4	29.22	31.15	21.40
6	3	7	1	11	3	29.32	30.96	21.32
6	3	8	1	13	4	29.54	31.06	21.22
6	3	9	1	21	5	29.63	31.06	21.56
6	3	10	1	25	4	29.64	31.08	21.49
6	3	11	1	27	4	29.78	31.15	21.50
6	3	12	1	24	4	29.82	31.20	21.62
6	3	13	1	44	5	29.86	31.28	21.38
6	3	14	1	45	4	29.06	30.04	21.38
6	3	15	1	48	4	29.97	31.35	21.51
6	3	16	1	48	4	30.09	31.40	21.50
6	3	17	1	46	4	30.22	31.44	21.50
6	3	18	1	49	4	30.33	31.74	21.35
6	3	19	1	36	3	30.98	32.37	21.18
6	3	20	1	32	4	30.62	31.62	21.62
6	3	21	1	32	4	30.76	31.65	21.26
6	3	22	1	32	4	30.92	32.28	21.49
6	3	23	1	28	4	30.98	31.72	21.32
6	3	24	1	33	4	31.03	31.81	21.54
6	3	25	1	27	3	31.03	31.75	21.41
6	3	26	2	16	3	30.06	31.46	21.20
6	3	27	2	12	4	30.08	31.61	21.45
6	3	28	2	16	4	30.17	31.57	21.31
6	3	29	2	9	3	30.18	31.65	21.49
6	3	30	2	9	4	30.29	31.66	21.62
6	3	31	2	10	4	30.26	31.81	21.56
6	3	32	2	8	4	30.40	31.87	21.53
6	3	33	2	2	3	30.46	31.95	21.63
6	3	34	2	0	4	30.60	32.08	21.42
6	3	35	2	0	4	30.72	32.11	21.54
7	1	0	0	1		26.66	33.24	21.46
7	1	1	0	3	5	26.63	33.24	21.59
7	1	2	0	46	5	26.59	33.23	21.63
7	1	3	0	50	4	26.62	33.24	21.40
7	1	4	0	59	5	26.52	33.24	21.71
7	1	5	0	64	5	26.66	33.35	21.54
7	1	6	1	43	3	17.32	25.19	21.36
7	1	7	1	36	3	14.50	17.61	21.40
7	1	8	1	34	4	12.85	14.59	21.53
7	1	9	1	24	3	11.76	12.73	21.40
7	1	10	1	39	5	10.76	11.45	21.36
7	1	11	1	33	3	9.98	10.84	21.55
7	1	12	1	30	4	9.30	10.18	21.47
7	1	13	1	34	4	8.76	9.68	21.32
7	1	14	1	35	4	8.18	9.40	21.47
7	1	15	1	40	5	7.47	9.18	21.54
7	1	16	1	34	4	6.76	8.64	21.36
7	1	17	1	34	4	6.64	8.78	21.55

Table C 14. Continued

7	1	18	1	42	5	5.73	8.06	21.44
7	1	19	1	41	4	5.39	7.71	21.45
7	1	20	1	44	3	5.09	7.48	21.45
7	1	21	1	28	3	4.85	7.30	21.42
7	1	22	1	19	3	4.63	7.27	21.51
7	1	23	1	29	4	4.40	7.07	21.60
7	1	24	1	29	4	4.26	6.99	21.74
7	1	25	1	30	4	4.09	6.91	21.63
7	1	26	2	33	4	7.87	11.57	21.71
7	1	27	2	30	4	9.11	13.94	21.51
7	1	28	2	10	3	10.07	16.12	21.58
7	1	29	2	10	4	10.67	18.06	21.64
7	1	30	2	2	3	11.21	19.73	21.60
7	1	31	2	2	3	11.79	21.08	21.87
7	1	32	2	2	2	12.22	22.10	22.07
7	1	33	2	3	4	12.67	22.89	21.82
7	1	34	2	1	4	13.12	23.51	21.50
7	1	35	2	2	4	13.50	24.18	21.64
8	3	0	0	0		28.21	31.62	21.76
8	3	1	0	2	5	28.10	31.70	21.80
8	3	2	0	2	4	28.21	31.76	21.73
8	3	3	0	19	5	28.51	31.94	21.62
8	3	4	0	32	5	27.97	31.87	21.78
8	3	5	0	22	3	28.06	31.85	21.68
8	3	6	1	25	4	27.20	31.29	21.55
8	3	7	1	23	4	27.31	31.20	21.71
8	3	8	1	10	3	27.42	31.23	21.60
8	3	9	1	30	5	27.47	31.30	21.55
8	3	10	1	37	5	27.51	31.42	21.59
8	3	11	1	44	5	27.60	31.36	21.82
8	3	12	1	49	5	27.63	31.60	21.83
8	3	13	1	50	4	27.69	31.66	21.90
8	3	14	1	47	4	27.74	31.69	21.63
8	3	15	1	47	3	27.79	31.79	21.72
8	3	16	1	36	3	27.83	31.91	21.65
8	3	17	1	56	5	27.85	31.87	21.85
8	3	18	1	59	4	27.92	32.05	21.68
8	3	19	1	63	3	27.96	32.09	21.58
8	3	20	1	61	3	28.05	32.20	21.55
8	3	21	1	50	3	28.08	32.28	21.54
8	3	22	1	51	4	28.14	32.35	21.86
8	3	23	1	54	4	28.21	32.40	21.80
8	3	24	1	46	3	28.25	32.50	21.83
8	3	25	1	47	4	28.28	32.54	21.71
8	3	26	2	44	4	27.75	32.08	21.56
8	3	27	2	44	3	27.87	32.04	21.64
8	3	28	2	34	3	26.67	32.02	21.80
8	3	29	2	28	3	27.96	32.06	21.82
8	3	30	2	23	3	27.93	32.18	21.77

Table C 14. Continued

8	3	31	2	12	3	27.38	31.92	21.82
8	3	32	2	4	3	27.74	32.26	21.78
8	3	33	2	1	3	28.02	32.29	21.74
8	3	34	2	1	3	27.63	32.28	21.56
8	3	35	2	0	3	28.17	32.50	21.64
9	3	0	0	0		26.17	31.13	21.89
9	3	1	0	7	5	26.23	31.19	21.80
9	3	2	0	7	5	27.04	31.04	21.91
9	3	3	0	7	5	26.68	30.87	21.82
9	3	4	0	9	5	26.38	30.80	21.90
9	3	5	0	15	5	26.48	30.91	21.83
9	3	6	1	12	3	26.68	30.06	21.89
9	3	7	1	18	5	26.81	30.01	21.99
9	3	8	1	12	4	26.89	30.20	21.91
9	3	9	1	13	4	26.92	30.33	21.81
9	3	10	1	13	4	26.95	30.53	21.95
9	3	11	1	14	4	27.02	30.71	21.82
9	3	12	1	13	3	27.04	30.82	21.86
9	3	13	1	13	4	27.11	31.00	21.87
9	3	14	1	12	3	27.10	31.09	21.90
9	3	15	1	13	5	27.16	31.24	21.85
9	3	16	1	15	4	27.20	31.37	21.80
9	3	17	1	10	3	27.22	31.46	21.92
9	3	18	1	8	4	27.26	31.55	21.86
9	3	19	1	13	5	27.25	31.49	21.89
9	3	20	1	12	4	27.31	31.71	21.82
9	3	21	1	10	3	27.34	31.76	21.82
9	3	22	1	9	3	27.39	31.85	21.83
9	3	23	1	13	4	27.42	31.91	21.86
9	3	24	1	10	4	27.48	32.01	21.86
9	3	25	1	13	5	27.45	32.05	21.74
9	3	26	2	13	4	27.25	31.59	21.82
9	3	27	2	11	3	27.11	31.75	21.73
9	3	28	2	10	3	27.17	31.94	21.92
9	3	29	2	8	3	27.13	31.96	21.98
9	3	30	2	6	3	27.26	32.11	21.95
9	3	31	2	6	3	27.12	32.20	21.89
9	3	32	2	4	3	27.17	32.37	21.87
9	3	33	2	3	3	27.15	32.42	21.89
9	3	34	2	5	3	27.17	32.50	21.95
9	3	35	2	3	4	27.15	32.58	22.01
10	1	0	0	0		28.17	32.51	21.80
10	1	1	0	18	5	28.19	32.56	21.94
10	1	2	0	26	5	28.91	32.67	21.72
10	1	3	0	39	5	28.65	32.69	21.82
10	1	4	0	49	4	28.68	32.74	21.91
10	1	5	0	70	5	28.65	32.76	21.91
10	1	6	1	59	3	12.73	19.94	21.90
10	1	7	1	65	5	8.28	14.77	21.91

Table C 14. Continued

10	1	8	1	47	3	9.23	16.92	21.92
10	1	9	1	64	5	9.53	12.86	21.94
10	1	10	1	73	5	8.14	10.23	21.87
10	1	11	1	75	4	7.98	8.95	21.87
10	1	12	1	51	3	8.25	8.37	21.99
10	1	13	1	34	3	7.75	7.85	21.91
10	1	14	1	44	5	7.91	7.30	21.95
10	1	15	1	40	4	7.10	7.31	21.85
10	1	16	1	24	3	6.89	6.94	21.83
10	1	17	1	27	4	6.27	6.72	21.92
10	1	18	1	41	5	5.58	6.61	21.89
10	1	19	1	42	4	5.31	6.37	21.85
10	1	20	1	42	4	5.80	5.84	21.89
10	1	21	1	42	4	5.61	6.20	21.95
10	1	22	1	15	3	5.72	5.47	21.94
10	1	23	1	14	4	5.60	5.51	21.99
10	1	24	1	10	4	5.31	6.68	22.00
10	1	25	1	41	5	5.47	7.11	21.50
10	1	26	2	27	3	8.67	10.83	21.96
10	1	27	2	21	4	9.89	12.22	21.86
10	1	28	2	20	4	10.74	14.84	21.81
10	1	29	2	21	4	11.52	16.12	22.00
10	1	30	2	11	3	12.22	18.62	21.98
10	1	31	2	9	4	12.78	20.36	22.01
10	1	32	2	9	4	13.43	21.31	22.03
10	1	33	2	2	3	14.09	22.05	21.89
10	1	34	2	2	4	14.59	22.64	21.95
10	1	35	2	4	4	15.06	23.12	21.83
11	3	0	0	0	5	28.91	32.28	21.78
11	3	1	0	6	5	28.97	32.24	21.82
11	3	2	0	12	5	29.04	32.40	21.77
11	3	3	0	27	5	29.04	32.29	21.80
11	3	4	0	32	5	29.24	32.24	21.69
11	3	5	0	46	5	29.30	32.29	21.85
11	3	6	1	46	4	28.48	31.56	21.80
11	3	7	1	57	5	28.52	31.36	21.86
11	3	8	1	56	4	28.46	31.41	21.81
11	3	9	1	57	4	28.56	31.51	21.65
11	3	10	1	55	4	28.59	31.64	21.68
11	3	11	1	48	3	28.66	31.72	21.81
11	3	12	1	48	4	28.70	31.79	21.90
11	3	13	1	42	3	28.74	31.84	21.80
11	3	14	1	54	4	28.83	31.95	21.73
11	3	15	1	57	5	28.88	32.01	21.80
11	3	16	1	58	4	28.95	32.10	21.74
11	3	17	1	57	4	29.01	32.19	21.73
11	3	18	1	49	3	29.07	32.26	21.76
11	3	19	1	58	5	29.13	32.35	21.87
11	3	20	1	60	5	29.20	32.41	21.85

Table C 14. Continued

11	3	21	1	60	5	29.25	32.49	21.81
11	3	22	1	53	3	29.32	32.53	21.81
11	3	23	1	52	4	29.37	32.59	21.77
11	3	24	1	60	5	29.45	32.67	21.81
11	3	25	1	62	5	29.50	32.77	21.87
11	3	26	2	66	5	29.24	32.63	21.72
11	3	27	2	63	4	29.75	32.38	21.63
11	3	28	2	52	3	30.35	32.41	21.81
11	3	29	2	50	4	30.80	32.53	21.74
11	3	30	2	50	4	31.20	32.69	21.83
11	3	31	2	41	3	31.47	32.82	21.77
11	3	32	2	32	3	31.79	32.94	21.68
11	3	33	2	20	3	31.96	33.08	21.82
11	3	34	2	20	4	32.24	33.19	21.85
11	3	35	2	14	3	32.38	33.30	21.73
12	2	0	0	0		28.77	31.79	21.72
12	2	1	0	7	5	28.95	32.14	21.62
12	2	2	0	0	3	28.71	32.13	21.80
12	2	3	0	0	4	28.73	32.31	21.90
12	2	4	0	0	4	28.68	32.47	21.77
12	2	5	0	0	4	28.65	32.55	21.82
12	2	6	1	3	4	13.66	17.98	21.58
12	2	7	1	15	5	10.14	10.07	21.55
12	2	8	1	17	5	7.89	7.82	21.80
12	2	9	1	20	3	6.64	6.50	21.73
12	2	10	1	21	3	5.72	5.87	21.89
12	2	11	1	25	4	5.65	5.51	21.92
12	2	12	1	21	4	5.30	5.26	21.85
12	2	13	1	23	4	5.34	5.05	21.72
12	2	14	1	20	4	5.05	4.89	21.81
12	2	15	1	23	4	4.22	4.70	21.85
12	2	16	1	19	4	4.23	4.39	21.77
12	2	17	1	18	4	3.90	4.27	21.82
12	2	18	1	13	4	3.63	4.12	21.76
12	2	19	1	17	4	3.55	4.16	21.81
12	2	20	1	18	4	3.38	4.03	21.71
12	2	21	1	26	4	3.30	4.07	21.69
12	2	22	1	19	4	3.25	3.97	21.86
12	2	23	1	18	4	3.23	3.80	21.85
12	2	24	1	17	4	3.23	3.67	21.77
12	2	25	1	14	4	2.51	3.70	21.83
12	2	26	2	17	4	7.48	8.55	21.76
12	2	27	2	15	4	8.95	10.57	21.73
12	2	28	2	9	3	10.07	12.09	21.80
12	2	29	2	4	3	10.86	13.54	21.82
12	2	30	2	5	3	11.61	15.01	21.86
12	2	31	2	6	3	12.31	16.32	21.60
12	2	32	2	3	3	13.19	17.53	21.83
12	2	33	2	3	3	14.09	18.54	21.81

Table C 14. Continued

12	2	34	2	3	4	15.22	19.46	21.74
12	2	35	2	3	4	15.90	20.28	21.80
13	2	0	0	0		29.23	31.64	21.89
13	2	1	0	3	4	29.13	31.80	21.81
13	2	2	0	3	4	29.18	31.92	21.85
13	2	3	0	1	4	29.14	32.02	21.81
13	2	4	0	2	4	29.16	32.17	21.78
13	2	5	0	1	4	29.11	32.28	21.76
13	2	6	1	20	5	20.19	21.83	21.83
13	2	7	1	20	4	12.96	11.71	21.67
13	2	8	1	23	5	9.99	8.09	21.72
13	2	9	1	25	4	9.38	6.54	21.76
13	2	10	1	25	4	8.74	5.62	21.68
13	2	11	1	25	4	8.24	5.16	21.69
13	2	12	1	27	4	7.44	4.86	21.76
13	2	13	1	22	4	6.33	4.54	21.80
13	2	14	1	25	3	5.68	4.32	21.59
13	2	15	1	23	4	5.24	4.20	21.80
13	2	16	1	23	4	4.92	4.09	21.54
13	2	17	1	24	4	4.68	4.04	21.71
13	2	18	1	21	4	4.43	4.04	21.68
13	2	19	1	18	4	4.15	3.99	21.78
13	2	20	1	21	3	4.12	3.85	21.65
13	2	21	1	21	4	3.80	3.94	21.68
13	2	22	1	21	3	3.55	3.99	21.46
13	2	23	1	21	4	3.47	4.09	21.76
13	2	24	1	17	3	3.36	3.97	21.45
13	2	25	1	14	3	3.02	3.82	21.77
13	2	26	2	14	3	6.89	9.91	21.89
13	2	27	2	13	3	8.56	12.10	21.68
13	2	28	2	11	3	9.48	14.12	21.73
13	2	29	2	5	3	10.32	16.23	21.62
13	2	30	2	0	3	11.01	17.86	21.65
13	2	31	2	0	4	11.80	19.05	21.63
13	2	32	2	0	4	12.24	19.96	21.63
13	2	33	2	0	4	12.74	20.70	21.69
13	2	34	2	0	4	13.23	21.44	21.62
13	2	35	2	0	4	13.82	22.05	21.58
14	1	0	0	0		28.05	32.86	21.72
14	1	1	0	3	5	28.05	32.96	21.68
14	1	2	0	10	5	28.08	33.00	21.80
14	1	3	0	11	4	27.97	33.04	21.69
14	1	4	0	22	5	27.94	33.04	21.69
14	1	5	0	31	5	27.97	33.13	21.55
14	1	6	1	33	5	14.42	26.72	20.56
14	1	7	1	33	4	7.86	21.72	21.69
14	1	8	1	36	4	6.45	18.35	21.62
14	1	9	1	26	3	5.77	16.03	21.63
14	1	10	1	28	4	5.12	14.42	21.83

Table C 14. Continued

14	1	11	1	28	3	4.62	13.09	21.55
14	1	12	1	17	3	4.30	12.18	21.64
14	1	13	1	15	3	4.05	11.25	21.71
14	1	14	1	8	3	3.84	10.53	21.67
14	1	15	1	15	4	3.65	9.91	21.72
14	1	16	1	5	3	3.53	9.45	21.68
14	1	17	1	4	4	3.42	9.11	21.56
14	1	18	1	4	4	3.25	8.78	21.55
14	1	19	1	4	4	3.09	8.48	21.74
14	1	20	1	10	5	3.04	8.21	21.62
14	1	21	1	12	4	2.97	7.95	21.63
14	1	22	1	6	3	3.02	7.75	21.63
14	1	23	1	6	3	2.93	7.61	21.63
14	1	24	1	2	3	2.85	7.44	21.63
14	1	25	1	3	4	2.81	7.36	21.67
14	1	26	2	1	3	6.24	11.25	21.64
14	1	27	2	0	3	7.79	12.70	21.67
14	1	28	2	0	4	9.22	13.98	21.67
14	1	29	2	2	4	10.22	15.16	21.63
14	1	30	2	1	5	10.97	16.03	21.69
14	1	31	2	2	4	11.78	17.05	21.59
14	1	32	2	6	4	12.31	17.80	21.63
14	1	33	2	6	5	12.98	18.62	21.49
14	1	34	2	4	4	13.46	19.26	21.59
14	1	35	2	8	4	13.96	19.94	21.72
15	1	0	0	0		28.34	32.56	21.68
15	1	1	0	2	5	28.15	32.14	21.51
15	1	2	0	9	5	28.03	32.15	21.50
15	1	3	0	40	5	27.99	32.23	21.67
15	1	4	0	40	4	27.87	32.19	21.65
15	1	5	0	43	5	27.83	32.18	21.10
15	1	6	1	32	3	24.00	20.25	21.80
15	1	7	1	32	4	18.80	10.72	21.35
15	1	8	1	25	3	16.00	8.20	21.50
15	1	9	1	19	3	14.29	7.10	21.63
15	1	10	1	11	3	12.66	6.76	21.54
15	1	11	1	10	4	11.66	6.37	21.59
15	1	12	1	6	4	11.49	6.20	21.50
15	1	13	1	6	3	10.68	5.91	21.41
15	1	14	1	5	4	9.65	5.74	21.73
15	1	15	1	4	3	9.65	5.64	21.23
15	1	16	1	3	3	9.07	5.74	21.40
15	1	17	1	2	4	8.64	5.83	21.23
15	1	18	1	4	3	8.10	5.74	21.38
15	1	19	1	3	4	7.50	5.85	21.18
15	1	20	1	2	3	6.83	5.95	21.28
15	1	21	1	3	3	6.64	5.83	21.40
15	1	22	1	2	4	6.18	5.76	21.36
15	1	23	1	2	4	5.97	5.76	21.26

Table C 14. Continued

15	1	24	1	3	3	5.93	5.69	20.91
15	1	25	1	1	3	6.38	5.57	21.49
15	1	26	2	1	3	8.29	9.91	21.49
15	1	27	2	1	3	9.51	11.76	21.35
15	1	28	2	1	4	10.05	13.27	21.20
15	1	29	2	1	4	10.98	14.59	21.46
15	1	30	2	0	3	11.40	15.70	21.55
15	1	31	2	0	3	11.99	16.82	21.49
15	1	32	2	0	4	12.36	17.74	21.33
15	1	33	2	1	5	12.86	18.62	21.87
15	1	34	2	1	5	13.27	19.49	21.71
15	1	35	2	1	4	13.63	20.18	22.04
16	1	0	0	0		30.45	33.89	21.78
16	1	1	0	6	5	30.38	34.05	21.69
16	1	2	0	8	4	30.56	34.14	21.71
16	1	3	0	19	5	30.42	34.02	21.51
16	1	4	0	24	4	30.51	34.05	21.72
16	1	5	0	22	5	30.49	34.18	21.71
16	1	6	1	10	3	25.64	26.08	21.36
16	1	7	1	7	3	16.43	10.99	21.56
16	1	8	1	9	4	13.27	10.22	21.50
16	1	9	1	9	3	11.26	10.44	21.72
16	1	10	1	4	3	9.44	9.41	21.83
16	1	11	1	5	4	8.29	9.18	21.77
16	1	12	1	3	3	6.91	8.32	21.81
16	1	13	1	5	4	6.19	7.32	21.67
16	1	14	1	5	4	5.31	6.81	21.53
16	1	15	1	7	4	4.73	6.46	21.72
16	1	16	1	10	4	4.34	6.22	21.74
16	1	17	1	9	4	4.19	6.10	21.44
16	1	18	1	12	4	3.80	5.50	21.63
16	1	19	1	9	3	3.17	5.01	21.54
16	1	20	1	5	3	3.35	5.18	21.72
16	1	21	1	4	3	2.92	5.03	21.71
16	1	22	1	4	4	3.25	5.14	21.55
16	1	23	1	2	3	3.05	5.53	21.65
16	1	24	1	1	3	2.86	5.31	21.91
16	1	25	1	4	5	3.38	5.61	21.72
16	1	26	2	5	4	5.32	9.66	21.73
16	1	27	2	1	3	7.43	12.93	21.55
16	1	28	2	1	4	9.20	14.04	21.74
16	1	29	2	2	4	9.91	16.00	21.83
16	1	30	2	0	3	11.09	17.98	21.80
16	1	31	2	0	4	11.95	19.34	21.82
16	1	32	2	0	3	12.50	19.93	21.81
16	1	33	2	0	4	13.35	21.29	21.56
16	1	34	2	0	4	14.14	21.95	21.90
16	1	35	2	0	3	15.05	22.98	21.72
17	1	0	0	0	5	28.59	32.69	21.78

Table C 14. Continued

17	1	1	0	5	5	28.60	32.69	21.83
17	1	2	0	11	5	28.44	32.67	21.51
17	1	3	0	28	5	27.90	32.63	21.81
17	1	4	0	50	5	28.15	32.60	21.78
17	1	5	0	61	5	28.05	32.56	21.62
17	1	6	1	56	4	21.73	23.29	21.91
17	1	7	1	54	4	13.01	18.23	21.67
17	1	8	1	54	3	10.21	15.48	21.73
17	1	9	1	44	4	8.52	13.23	21.85
17	1	10	1	63	5	7.18	9.09	21.77
17	1	11	1	62	5	6.75	7.46	21.56
17	1	12	1	74	5	5.89	6.50	21.67
17	1	13	1	72	5	5.42	6.12	21.72
17	1	14	1	85	5	5.01	5.91	21.69
17	1	15	1	83	5	4.70	5.62	21.58
17	1	16	1	80	4	4.34	5.37	21.58
17	1	17	1	82	4	4.23	5.54	21.73
17	1	18	1	84	5	4.03	5.65	21.65
17	1	19	1	81	4	3.86	5.66	21.68
17	1	20	1	83	4	3.76	5.72	21.65
17	1	21	1	84	4	3.48	5.87	21.37
17	1	22	1	81	4	3.57	5.65	21.78
17	1	23	1	74	3	3.46	5.50	21.71
17	1	24	1	67	3	3.31	5.43	21.69
17	1	25	1	67	4	4.51	6.95	21.73
17	1	26	2	62	3	6.87	10.06	21.63
17	1	27	2	55	4	8.59	12.27	21.65
17	1	28	2	53	3	9.61	14.42	21.74
17	1	29	2	46	4	10.72	16.16	21.72
17	1	30	2	37	3	11.55	17.42	21.81
17	1	31	2	33	3	12.22	18.58	21.71
17	1	32	2	27	4	12.96	19.70	21.68
17	1	33	2	22	4	13.59	20.55	21.67
17	1	34	2	18	4	14.10	21.37	21.65
17	1	35	2	19	3	14.64	22.09	21.77
18	1	0	0	0		30.05	31.64	21.71
18	1	1	0	2	5	29.73	31.86	21.69
18	1	2	0	2	4	29.93	32.02	21.47
18	1	3	0	6	5	29.87	32.24	21.50
18	1	4	0	10	5	29.84	32.38	21.72
18	1	5	0	13	5	30.05	32.24	21.63
18	1	6	1	12	5	21.19	17.84	21.90
18	1	7	1	25	5	15.86	12.60	21.50
18	1	8	1	41	4	12.12	9.52	21.60
18	1	9	1	39	4	10.15	7.95	21.73
18	1	10	1	40	4	9.48	7.00	21.56
18	1	11	1	46	5	8.17	6.54	21.54
18	1	12	1	43	4	7.27	6.16	21.68
18	1	13	1	43	4	6.54	5.93	21.56

Table C 14. Continued

18	1	14	1	44	4	5.97	5.70	21.74
18	1	15	1	41	4	5.53	5.77	21.62
18	1	16	1	46	5	5.22	5.42	21.65
18	1	17	1	46	4	4.69	5.24	21.60
18	1	18	1	44	4	4.47	5.14	21.68
18	1	19	1	44	4	4.31	5.03	21.32
18	1	20	1	50	5	4.09	4.85	21.47
18	1	21	1	40	4	3.85	4.91	21.67
18	1	22	1	46	4	3.62	4.76	21.64
18	1	23	1	49	5	3.61	4.73	21.53
18	1	24	1	51	4	3.36	4.59	21.56
18	1	25	1	51	5	3.04	4.31	21.71
18	1	26	2	52	3	6.14	12.16	21.58
18	1	27	2	43	3	7.56	14.36	21.56
18	1	28	2	30	3	8.49	15.58	21.86
18	1	29	2	14	3	9.24	17.12	21.67
18	1	30	2	8	3	10.09	18.68	22.01
18	1	31	2	7	4	10.80	19.97	21.86
18	1	32	2	7	3	11.48	20.63	21.89
18	1	33	2	5	4	12.04	21.18	21.77
18	1	34	2	4	3	12.48	21.54	21.63
18	1	35	2	5	3	13.02	21.98	21.80
19	2	0	0	0		26.90	31.06	21.55
19	2	1	0	1	4	27.04	31.23	21.63
19	2	2	0	1	4	27.11	31.54	21.46
19	2	3	0	1	4	27.13	31.66	21.56
19	2	4	0	0	4	27.19	31.76	21.47
19	2	5	0	0	5	27.25	31.87	21.54
19	2	6	1	14	5	23.60	17.82	21.51
19	2	7	1	10	5	19.60	10.80	21.60
19	2	8	1	20	5	16.19	7.87	21.23
19	2	9	1	15	3	16.19	6.23	21.31
19	2	10	1	13	3	15.03	5.81	21.62
19	2	11	1	15	4	14.72	5.60	21.27
19	2	12	1	17	3	13.39	5.55	21.72
19	2	13	1	15	3	12.51	5.47	21.41
19	2	14	1	13	4	11.82	5.43	21.42
19	2	15	1	17	4	10.92	5.54	21.37
19	2	16	1	13	3	10.19	5.55	21.68
19	2	17	1	13	4	9.89	5.51	20.97
19	2	18	1	13	4	9.47	5.65	21.23
19	2	19	1	11	3	8.95	5.73	21.27
19	2	20	1	13	3	8.30	5.84	21.44
19	2	21	1	9	3	7.99	5.88	21.45
19	2	22	1	12	4	7.63	5.77	21.32
19	2	23	1	10	3	7.28	5.77	21.44
19	2	24	1	10	3	7.03	5.62	21.23
19	2	25	1	8	3	6.85	5.50	21.36
19	2	26	2	8	3	8.62	9.91	21.50

Table C 14. Continued

19	2	27	2	1	3	9.93	11.98	21.26
19	2	28	2	0	3	10.53	13.37	21.46
19	2	29	2	0	3	11.22	14.72	21.42
19	2	30	2	0	4	11.70	15.92	21.29
19	2	31	2	0	4	12.05	16.71	21.44
19	2	32	2	0	4	12.54	17.56	21.37
19	2	33	2	0	4	12.89	18.51	21.33
19	2	34	2	0	4	13.20	19.28	21.35
19	2	35	2	0	4	13.51	19.94	21.45
20	1	0	0	0		27.24	33.62	21.36
20	1	1	0	2	5	27.21	33.73	21.15
20	1	2	0	7	5	27.12	33.94	21.20
20	1	3	0	15	5	27.17	33.75	21.06
20	1	4	0	22	5	27.10	33.54	21.36
20	1	5	0	33	5	27.17	33.30	21.20
20	1	6	1	37	5	21.14	19.70	21.45
20	1	7	1	49	5	16.26	12.09	21.41
20	1	8	1	62	5	13.33	9.22	21.20
20	1	9	1	58	5	11.03	7.75	21.42
20	1	10	1	61	4	9.85	7.34	21.42
20	1	11	1	61	4	8.72	6.88	21.32
20	1	12	1	50	3	7.73	6.35	21.31
20	1	13	1	48	4	6.88	6.00	21.32
20	1	14	1	48	3	6.22	5.74	21.31
20	1	15	1	45	3	5.61	5.34	21.23
20	1	16	1	43	3	5.12	5.12	21.20
20	1	17	1	44	4	4.81	4.97	21.15
20	1	18	1	45	4	4.54	4.77	21.11
20	1	19	1	41	3	4.32	4.62	21.45
20	1	20	1	37	4	3.93	4.26	21.27
20	1	21	1	44	3	3.76	4.39	21.09
20	1	22	1	37	4	3.57	4.24	21.41
20	1	23	1	37	3	3.43	4.23	21.26
20	1	24	1	35	4	3.25	4.07	21.27
20	1	25	1	50	5	3.12	3.92	21.24
20	1	26	2	28	3	6.30	9.99	21.26
20	1	27	2	27	3	7.73	13.27	21.17
20	1	28	2	23	3	8.66	16.18	21.31
20	1	29	2	23	3	9.44	18.64	21.28
20	1	30	2	3	3	10.18	19.80	21.22
20	1	31	2	0	3	10.94	20.02	21.26
20	1	32	2	0	4	11.41	20.23	21.33
20	1	33	2	0	4	11.91	20.38	21.27
20	1	34	2	1	3	12.32	20.51	21.35
20	1	35	2	0	4	12.79	20.76	21.37
21	3	0	0	0		28.28	33.86	21.80
21	3	1	0	0	4	28.26	33.89	21.80
21	3	2	0	0	4	28.20	33.98	21.54
21	3	3	0	2	5	28.21	34.10	21.60

Table C 14. Continued

21	3	4	0	2	4	28.17	34.14	21.60
21	3	5	0	7	5	28.42	33.03	21.89
21	3	6	1	7	4	27.66	32.36	21.73
21	3	7	1	12	5	27.70	32.19	21.59
21	3	8	1	15	4	27.66	32.14	21.42
21	3	9	1	21	5	27.65	32.40	21.51
21	3	10	1	21	4	27.69	32.76	21.54
21	3	11	1	25	5	27.69	32.78	21.69
21	3	12	1	22	3	27.76	33.01	21.51
21	3	13	1	27	5	27.69	33.01	21.77
21	3	14	1	25	5	27.70	33.15	21.65
21	3	15	1	33	5	27.71	33.24	21.63
21	3	16	1	34	5	27.72	33.28	21.67
21	3	17	1	37	5	27.72	33.37	21.64
21	3	18	1	39	4	27.72	33.46	21.72
21	3	19	1	37	4	27.74	33.41	21.73
21	3	20	1	42	5	27.74	33.46	21.69
21	3	21	1	49	5	27.76	33.46	21.74
21	3	22	1	50	4	27.78	33.54	21.68
21	3	23	1	51	5	27.81	33.60	21.63
21	3	24	1	55	5	27.87	33.72	21.73
21	3	25	1	54	4	28.07	33.50	21.71
21	3	26	2	64	5	27.65	33.31	21.54
21	3	27	2	67	4	27.67	33.22	21.58
21	3	28	2	69	5	27.78	33.24	21.68
21	3	29	2	30	4	27.76	33.30	21.67
21	3	30	2	30	4	27.79	33.40	21.80
21	3	31	2	30	4	27.84	33.40	21.81
21	3	32	2	31	3	27.84	33.36	21.71
21	3	33	2	30	3	27.85	33.55	21.65
21	3	34	2	15	4	27.92	33.73	21.71
21	3	35	2	13	3	27.98	33.76	21.67
22	3	0	0	0		28.68	31.96	21.72
22	3	1	0	1	5	28.61	32.17	21.86
22	3	2	0	36	5	28.39	32.02	21.83
22	3	3	0	52	5	28.08	31.87	21.89
22	3	4	0	62	5	28.01	31.94	21.81
22	3	5	0	65	5	27.79	32.05	21.62
22	3	6	1	72	4	28.16	30.78	21.85
22	3	7	1	74	4	28.44	31.44	21.92
22	3	8	1	72	5	28.47	31.69	21.89
22	3	9	1	70	3	28.61	31.97	21.92
22	3	10	1	81	6	28.70	32.15	21.77
22	3	11	1	82	4	28.77	32.35	21.82
22	3	12	1	75	3	28.84	32.50	21.85
22	3	13	1	63	3	28.91	32.67	21.71
22	3	14	1	49	3	29.00	32.74	21.86
22	3	15	1	50	3	29.05	32.87	21.59
22	3	16	1	45	3	29.10	32.96	21.89

Table C 14. Continued

22	3	17	1	32	3	29.15	33.06	21.87
22	3	18	1	31	4	28.89	32.99	21.80
22	3	19	1	22	3	29.20	33.18	21.90
22	3	20	1	25	4	29.34	33.32	21.86
22	3	21	1	26	4	29.39	33.35	21.68
22	3	22	1	24	3	29.42	33.44	21.59
22	3	23	1	21	3	29.51	33.48	21.24
22	3	24	1	20	3	29.54	33.55	21.59
22	3	25	1	12	3	29.57	33.57	21.56
22	3	26	2	14	3	28.98	32.82	21.38
22	3	27	2	10	3	29.02	32.94	21.59
22	3	28	2	7	3	28.93	32.92	21.55
22	3	29	2	6	3	29.02	32.96	21.56
22	3	30	2	2	3	29.09	33.03	21.58
22	3	31	2	2	3	29.07	33.09	21.53
22	3	32	2	1	3	29.10	33.13	21.56
22	3	33	2	0	3	29.06	33.19	21.55
22	3	34	2	0	4	29.13	33.28	21.58
22	3	35	2	0	4	29.16	33.35	21.73
23	2	0	0	0	5	28.20	31.94	21.77
23	2	1	0	6	3	28.15	32.08	21.91
23	2	2	0	6	4	28.24	32.28	21.89
23	2	3	0	6	3	28.26	32.42	21.86
23	2	4	0	7	3	28.26	32.56	21.78
23	2	5	0	5	3	23.04	28.97	21.73
23	2	6	1	1	3	17.55	18.02	21.87
23	2	7	1	1	3	14.38	14.40	21.77
23	2	8	1	1	4	12.01	12.62	21.86
23	2	9	1	1	4	10.59	11.38	21.82
23	2	10	1	3	5	9.23	10.67	21.78
23	2	11	1	2	4	8.40	10.02	21.81
23	2	12	1	3	4	7.69	9.51	21.83
23	2	13	1	2	4	6.83	9.17	21.85
23	2	14	1	2	4	6.20	8.86	21.69
23	2	15	1	1	3	5.80	8.67	21.72
23	2	16	1	1	4	5.47	8.55	21.83
23	2	17	1	1	3	5.22	8.59	21.77
23	2	18	1	1	4	4.88	8.63	21.77
23	2	19	1	1	4	4.63	8.62	21.77
23	2	20	1	1	4	4.40	8.55	21.68
23	2	21	1	1	4	4.39	8.20	21.71
23	2	22	1	1	4	4.09	7.98	21.76
23	2	23	1	0	3	3.88	7.90	21.81
23	2	24	1	1	4	3.78	7.90	21.80
23	2	25	1	0	4	8.24	11.94	21.82
23	2	26	2	1	4	9.78	13.21	21.82
23	2	27	2	1	4	10.69	14.59	21.87
23	2	28	2	1	4	11.60	15.96	21.86
23	2	29	2	1	4	12.24	17.35	21.74

Table C 14. Continued

23	2	30	2	0	3	12.86	18.75	21.90
23	2	31	2	0	4	13.32	20.01	21.74
23	2	32	2	0	4	13.82	21.15	21.89
23	2	33	2	0	4	14.40	22.25	21.80
23	2	34	2	0	4	14.76	23.14	21.82
23	2	35	2	0	4	15.20	24.04	21.90
24	3	0	0	0		29.16	33.58	22.04
24	3	1	0	1	5	29.04	33.49	22.14
24	3	2	0	9	5	28.98	33.42	22.08
24	3	3	0	19	5	28.93	33.45	22.09
24	3	4	0	24	5	28.89	33.51	21.89
24	3	5	0	42	5	28.70	33.73	22.08
24	3	6	1	35	3	28.10	32.78	22.13
24	3	7	1	29	3	28.12	32.61	22.16
24	3	8	1	28	4	28.12	32.50	22.04
24	3	9	1	43	5	28.14	32.42	22.12
24	3	10	1	63	5	28.14	32.41	22.07
24	3	11	1	70	5	28.15	32.54	22.19
24	3	12	1	75	5	28.12	32.61	22.09
24	3	13	1	76	5	28.10	32.70	22.10
24	3	14	1	78	5	28.02	32.79	22.09
24	3	15	1	71	3	28.12	32.99	22.08
24	3	16	1	66	3	28.06	33.04	22.08
24	3	17	1	72	5	28.02	33.10	22.07
24	3	18	1	71	4	28.05	33.26	22.04
24	3	19	1	67	3	28.06	33.39	22.10
24	3	20	1	70	4	28.07	33.48	22.00
24	3	21	1	71	5	28.12	33.53	22.01
24	3	22	1	71	3	28.15	33.59	21.98
24	3	23	1	63	3	28.19	33.64	22.07
24	3	24	1	66	3	28.17	33.50	22.08
24	3	25	1	58	3	28.50	33.67	22.07
24	3	26	2	62	4	27.90	32.58	22.16
24	3	27	2	60	3	27.90	33.21	22.08
24	3	28	2	53	3	27.92	33.69	22.10
24	3	29	2	30	3	27.98	34.10	22.08
24	3	30	2	13	3	27.96	34.29	22.08
24	3	31	2	13	3	27.94	34.48	22.07
24	3	32	2	11	3	27.96	34.61	22.14
24	3	33	2	5	3	27.97	34.74	22.10
24	3	34	2	5	3	27.99	34.75	22.05
24	3	35	2	3	3	27.98	34.79	22.03
25	2	0	0	0		28.14	31.28	21.68
25	2	1	0	1	4	27.57	31.35	21.37
25	2	2	0	1	4	27.62	31.44	21.67
25	2	3	0	1	4	27.57	31.56	21.54
25	2	4	0	1	4	27.54	31.70	21.53
25	2	5	0	1	4	27.45	31.92	21.40
25	2	6	1	2	5	10.10	20.61	21.19

Table C 14. Continued

25	2	7	1	3	4	9.19	9.51	21.40
25	2	8	1	3	4	7.62	6.62	21.29
25	2	9	1	3	5	6.53	5.53	21.42
25	2	10	1	4	4	5.93	5.23	21.33
25	2	11	1	4	5	4.99	4.73	21.38
25	2	12	1	5	4	4.55	4.61	21.20
25	2	13	1	8	5	4.35	4.63	21.22
25	2	14	1	8	4	3.97	4.32	21.38
25	2	15	1	10	4	3.73	4.47	21.37
25	2	16	1	11	4	3.43	4.61	21.27
25	2	17	1	10	4	3.23	4.61	21.26
25	2	18	1	10	4	3.00	4.34	21.31
25	2	19	1	9	3	2.90	4.27	21.33
25	2	20	1	8	4	2.74	4.22	21.38
25	2	21	1	8	4	2.78	4.27	21.47
25	2	22	1	5	3	2.69	4.30	21.47
25	2	23	1	0	3	2.69	4.24	21.59
25	2	24	1	0	4	2.56	4.20	21.31
25	2	25	1	0	4	3.19	3.88	21.64
25	2	26	2	0	4	5.57	9.41	21.56
25	2	27	2	0	4	7.14	12.28	21.33
25	2	28	2	1	4	8.25	15.14	21.28
25	2	29	2	0	4	8.99	17.55	21.46
25	2	30	2	0	4	9.82	19.25	21.26
25	2	31	2	0	4	10.78	20.47	21.33
25	2	32	2	0	4	11.53	21.44	21.31
25	2	33	2	0	4	12.22	22.32	21.59
25	2	34	2	0	4	12.97	23.04	21.47
25	2	35	2	0	4	13.89	23.79	21.41
26	3	0	0	0		28.83	32.06	21.44
26	3	1	0	0	4	28.77	32.14	21.37
26	3	2	0	0	4	28.75	32.22	21.28
26	3	3	0	8	5	28.46	32.56	21.36
26	3	4	0	9	4	28.62	31.74	21.32
26	3	5	0	13	5	28.68	31.37	21.20
26	3	6	1	14	4	28.79	31.31	21.46
26	3	7	1	16	5	29.87	31.08	21.44
26	3	8	1	17	4	28.84	31.20	21.28
26	3	9	1	20	5	28.91	31.25	21.26
26	3	10	1	23	4	28.97	31.31	21.36
26	3	11	1	25	4	28.97	31.34	21.20
26	3	12	1	31	5	28.98	31.36	21.36
26	3	13	1	32	4	29.11	31.46	21.24
26	3	14	1	34	5	29.06	31.46	21.51
26	3	15	1	36	4	29.11	31.59	21.37
26	3	16	1	37	4	30.18	31.72	21.19
26	3	17	1	43	4	29.15	31.69	21.46
26	3	18	1	42	4	29.15	31.72	21.54
26	3	19	1	41	4	29.19	31.79	21.37

Table C 14. Continued

26	3	20	1	42	4	29.20	31.84	21.17
26	3	21	1	42	4	29.22	31.89	21.23
26	3	22	1	40	4	29.24	31.94	21.33
26	3	23	1	52	5	29.15	32.09	21.42
26	3	24	1	45	4	28.77	31.71	21.59
26	3	25	1	48	4	28.82	31.89	21.09
26	3	26	2	45	4	28.52	31.80	21.46
26	3	27	2	44	4	28.62	32.00	21.46
26	3	28	2	44	4	28.66	32.11	21.35
26	3	29	2	46	4	28.66	32.19	21.53
26	3	30	2	37	4	28.53	32.33	21.41
26	3	31	2	35	4	28.60	32.44	21.51
26	3	32	2	28	4	28.62	32.54	21.60
26	3	33	2	18	4	28.65	32.73	21.40
26	3	34	2	17	4	28.60	32.76	21.65
26	3	35	2	14	3	28.60	32.74	21.62
27	2	0	0	0		26.88	31.19	21.91
27	2	1	0	8	5	26.79	31.34	21.56
27	2	2	0	8	3	26.86	31.62	21.54
27	2	3	0	4	3	26.80	31.80	21.55
27	2	4	0	4	3	26.89	31.92	21.86
27	2	5	0	2	3	26.89	31.94	21.53
27	2	6	1	3	5	20.45	20.43	21.71
27	2	7	1	21	5	15.51	11.67	21.53
27	2	8	1	21	3	12.39	9.19	21.53
27	2	9	1	17	4	9.95	7.62	21.50
27	2	10	1	11	3	8.05	6.23	21.54
27	2	11	1	13	4	6.70	5.49	21.64
27	2	12	1	6	3	5.88	4.86	21.60
27	2	13	1	7	4	5.50	4.31	21.47
27	2	14	1	8	4	5.14	4.46	21.47
27	2	15	1	8	4	4.74	4.42	21.47
27	2	16	1	7	4	4.35	4.43	21.58
27	2	17	1	9	4	4.05	4.49	21.51
27	2	18	1	9	4	3.76	4.62	21.53
27	2	19	1	11	4	3.53	4.77	21.68
27	2	20	1	9	4	3.32	4.77	21.58
27	2	21	1	10	4	3.16	4.66	21.49
27	2	22	1	10	4	3.07	4.51	21.59
27	2	23	1	13	4	2.97	4.43	21.68
27	2	24	1	10	4	2.86	4.40	21.58
27	2	25	1	13	4	3.51	5.80	21.73
27	2	26	2	11	3	7.52	9.40	21.62
27	2	27	2	4	3	8.68	11.68	21.54
27	2	28	2	3	3	9.53	13.96	21.67
27	2	29	2	1	3	10.45	16.18	21.26
27	2	30	2	1	4	11.05	18.05	21.50
27	2	31	2	1	3	11.90	19.32	21.64
27	2	32	2	1	4	12.24	20.74	21.64

Table C 14. Continued

27	2	33	2	1	4	12.83	21.62	21.64
27	2	34	2	1	4	13.17	22.40	21.58
27	2	35	2	1	4	13.59	23.01	21.68
28	2	0	0	3	5	30.01	32.53	22.07
28	2	1	0	8	3	29.96	32.65	21.96
28	2	2	0	6	4	29.82	32.72	22.08
28	2	3	0	6	4	29.74	32.74	21.81
28	2	4	0	4	4	29.56	32.63	22.08
28	2	5	0	4	4	25.15	25.06	21.71
28	2	6	1	4	4	17.74	15.19	22.01
28	2	7	1	9	5	14.34	10.91	22.03
28	2	8	1	12	5	11.63	8.37	22.19
28	2	9	1	11	4	9.97	7.04	22.18
28	2	10	1	8	3	8.22	6.31	22.17
28	2	11	1	7	3	7.31	5.93	21.98
28	2	12	1	5	3	5.95	5.60	22.17
28	2	13	1	5	4	5.77	5.42	22.08
28	2	14	1	5	4	5.19	5.35	22.08
28	2	15	1	4	4	4.54	5.19	22.09
28	2	16	1	4	4	4.09	5.19	22.10
28	2	17	1	5	4	3.85	5.18	22.16
28	2	18	1	5	4	3.76	5.22	22.10
28	2	19	1	4	4	3.61	5.28	22.05
28	2	20	1	5	4	3.40	5.32	22.14
28	2	21	1	5	4	3.30	5.35	21.92
28	2	22	1	5	4	3.11	5.41	22.08
28	2	23	1	4	4	3.02	5.53	22.19
28	2	24	1	5	4	2.93	5.46	22.05
28	2	25	1	4	4	6.38	10.60	22.04
28	2	26	2	4	4	7.36	13.36	22.03
28	2	27	2	3	3	8.21	16.32	22.16
28	2	28	2	3	4	9.32	19.12	22.17
28	2	29	2	3	4	10.30	20.88	22.01
28	2	30	2	0	4	11.59	21.81	21.99
28	2	31	2	0	4	12.83	22.66	21.95
28	2	32	2	0	4	14.15	23.35	22.16
28	2	33	2	0	4	15.31	24.02	22.19
28	2	34	2	0	4	16.35	24.64	22.07
28	2	35	2	0	4	17.40	25.22	21.92
29	1	0	0	0		27.94	31.60	21.92
29	1	1	0	2	5	27.87	31.79	21.72
29	1	2	0	18	5	27.83	31.77	21.81
29	1	3	0	57	5	27.76	31.97	21.83
29	1	4	0	58	5	27.61	32.10	21.72
29	1	5	0	75	5	27.58	32.28	21.89
29	1	6	1	55	3	21.96	26.29	21.72
29	1	7	1	60	4	15.31	17.89	21.53
29	1	8	1	60	4	12.05	13.59	21.81
29	1	9	1	58	4	10.18	11.36	21.80

Table C 14. Continued

29	1	10	1	46	3	8.87	9.70	21.82
29	1	11	1	46	3	7.71	8.70	21.83
29	1	12	1	44	4	7.18	8.01	21.87
29	1	13	1	43	3	6.54	7.52	21.81
29	1	14	1	38	3	6.06	7.27	21.77
29	1	15	1	26	3	5.55	6.96	21.92
29	1	16	1	24	3	5.14	6.69	21.81
29	1	17	1	27	4	4.89	6.58	21.82
29	1	18	1	32	5	4.61	6.31	21.83
29	1	19	1	27	3	4.40	6.03	21.81
29	1	20	1	17	3	4.28	5.76	21.92
29	1	21	1	16	3	4.17	5.68	21.92
29	1	22	1	12	3	3.97	5.55	21.86
29	1	23	1	10	4	3.81	5.51	21.89
29	1	24	1	8	4	3.66	5.46	21.78
29	1	25	1	6	3	3.89	5.31	21.11
29	1	26	2	3	3	7.54	10.33	21.72
29	1	27	2	0	3	8.70	13.08	21.82
29	1	28	2	1	4	9.78	14.84	21.85
29	1	29	2	1	4	10.60	16.52	21.87
29	1	30	2	0	4	12.24	18.07	21.87
29	1	31	2	0	4	12.17	18.54	21.82
29	1	32	2	0	4	13.04	19.94	21.85
29	1	33	2	0	4	13.65	20.68	21.59
29	1	34	2	0	4	14.27	21.23	21.78
29	1	35	2	0	4	14.88	21.67	21.89
30	2	0	0	0		29.16	33.85	21.72
30	2	1	0	6	5	29.15	34.00	21.74
30	2	2	0	3	3	29.19	34.03	21.76
30	2	3	0	3	3	29.05	34.18	21.71
30	2	4	0	4	4	29.06	34.24	21.54
30	2	5	0	2	3	22.36	20.63	21.26
30	2	6	1	22	5	15.91	12.96	21.74
30	2	7	1	40	5	10.91	9.89	21.83
30	2	8	1	45	4	8.59	8.78	21.65
30	2	9	1	25	3	7.40	7.73	21.81
30	2	10	1	31	5	6.66	7.19	21.60
30	2	11	1	34	3	6.12	6.46	21.80
30	2	12	1	26	3	5.72	5.95	21.65
30	2	13	1	30	4	5.30	5.68	21.49
30	2	14	1	24	3	5.01	5.50	21.77
30	2	15	1	28	4	4.74	5.24	21.82
30	2	16	1	22	3	4.51	5.15	21.46
30	2	17	1	23	4	4.38	4.97	21.37
30	2	18	1	20	4	4.27	4.91	21.87
30	2	19	1	15	4	4.09	4.84	21.60
30	2	20	1	18	4	4.00	4.70	21.74
30	2	21	1	16	4	3.97	4.55	21.73
30	2	22	1	12	3	3.96	4.50	21.67

Table C 14. Continued

30	2	23	1	9	3	3.96	4.36	21.71
30	2	24	1	13	4	4.11	4.47	21.56
30	2	25	1	14	4	6.46	9.39	21.82
30	2	26	2	3	3	8.05	13.25	21.77
30	2	27	2	2	3	8.98	16.57	21.81
30	2	28	2	2	4	9.69	18.91	21.19
30	2	29	2	1	3	10.45	20.93	21.71
30	2	30	2	0	3	11.01	22.13	21.41
30	2	31	2	1	4	11.97	23.46	21.51
30	2	32	2	1	4	12.63	24.14	21.58
30	2	33	2	1	4	13.62	24.97	21.73
30	2	34	2	1	4	14.01	25.33	21.80
30	2	35	2	1	4	14.63	25.86	21.58

Sub = subject
Cond = condition
VAS = visual analogue scale
Pat. = patella surface temperature
Pop. = popliteal surface temperature
Amb. = ambient temperature

Experiment II

Table C 15. H_{max} Measure for Each Condition Across Time. Measures were Taken Before, Immediately After, and 30 Minutes Following Each of the 4 Conditions (n = 3 Measures/Condition; Mean ± SD)

Condition	Pre	$Post_{tx}$ ‡	30 min $post_{tx}$ ‡
Saline*	2.6 ± 1.5	1.7 ± 1.6	1.7 ± 1.4
Saline/cryo†	3.1 ± 1.2	4.2 ± 1.2	3.1 ± 1.5
Saline/sham*	2.8 ± 1.6	1.7 ± 1.7	1.9 ± 1.9
No saline	3.4 ± 2.3	3.4 ± 2.3	3.4 ± 2.2

*Pre > post and 30 post

†Post > pre and 30 post

‡Saline/cryo and no saline > saline and saline/sham

Table C 16. Mixed Model Procedures for Fixed Effects Differences Between Condition and Time for the H_{max}

Effect	Numerator Degrees of Freedom	Denominator Degrees of Freedom	F-value	*P*-value
Time	2	72	5.8	.005*
Condi	3	72	2.3	.09
Cond x Time	6	72	8.7	<.0001*

* = represents a significant difference

Table C 17. Least Means Squares Differences for the H_{max}

Effect	Cond	Time	Cond	Time	t-value	DF	*P*-value
Cond x Time	Saline	Pre	Saline	Post	3.58	72	.0006*
Cond x Time	Saline	Pre	Saline	30 post	3.59	72	.0006*
Cond x Time	Saline	Pre	Saline/cryo	Pre	-0.55	72	.58
Cond x Time	Saline	Pre	Saline/cryo	Post	-0.58	72	.04*
Cond x Time	Saline	Pre	Saline/cryo	30 post	-0.27	72	.56
Cond x Time	Saline	Pre	Saline/sham	Pre	1.23	72	.79
Cond x Time	Saline	Pre	Saline/sham	Post	0.95	72	.22
Cond x Time	Saline	Pre	Saline/sham	30 post	-1.00	72	.35
Cond x Time	Saline	Pre	No saline	Pre	-0.97	72	.32
Cond x Time	Saline	Pre	No saline	Post	-1.06	72	.34
Cond x Time	Saline	Pre	No saline	30 post	0.01	72	.29
Cond x Time	Saline	Post	Saline	30 post	-1.79	72	.99
Cond x Time	Saline	Post	Saline/cryo	Pre	-3.32	72	.08
Cond x Time	Saline	Post	Saline/cryo	Post	-1.82	72	.001*
Cond x Time	Saline	Post	Saline/cryo	30 post	-1.51	72	.07
Cond x Time	Saline	Post	Saline/sham	Pre	-0.01	72	.14
Cond x Time	Saline	Post	Saline/sham	Post	-0.29	72	.99
Cond x Time	Saline	Post	Saline/sham	30 post	-2.24	72	.77
Cond x Time	Saline	Post	No saline	Pre	-2.20	72	.03*
Cond x Time	Saline	Post	No saline	Post	-2.30	72	.03*
Cond x Time	Saline	Post	No saline	30 post	-1.80	72	.02*
Cond x Time	Saline	30 post	Saline/cryo	Pre	-3.32	72	.08
Cond x Time	Saline	30 post	Saline/cryo	Post	-1.82	72	.001*
Cond x Time	Saline	30 post	Saline/cryo	30 post	-1.51	72	.07
Cond x Time	Saline	30 post	Saline/sham	Pre	-0.02	72	.14
Cond x Time	Saline	30 post	Saline/sham	Post	-0.30	72	.99
Cond x Time	Saline	30 post	Saline/sham	30 post	-2.24	72	.77
Cond x Time	Saline	30 post	No saline	Pre	-2.21	72	.03*
Cond x Time	Saline	30 post	No saline	Post	-2.31	72	.03*
Cond x Time	Saline	30 post	No saline	30 post	-4.40	72	.02*
Cond x Time	Saline/cryo	Pre	Saline/cryo	Post	-0.08	72	<.0001*
Cond x Time	Saline/cryo	Pre	Saline/cryo	30 post	0.29	72	.94
Cond x Time	Saline/cryo	Pre	Saline/sham	Pre	1.78	72	.78
Cond x Time	Saline/cryo	Pre	Saline/sham	Post	1.50	72	.08
Cond x Time	Saline/cryo	Pre	Saline/sham	30 post	-0.44	72	.14
Cond x Time	Saline/cryo	Pre	No saline	Pre	-0.41	72	.66
Cond x Time	Saline/cryo	Pre	No saline	Post	-0.51	72	.68
Cond x Time	Saline/cryo	Pre	No saline	30 post	4.33	72	.61
Cond x Time	Saline/cryo	Post	Saline/cryo	30 post	1.81	72	<.0001*
Cond x Time	Saline/cryo	Post	Saline/sham	Pre	3.31	72	.07
Cond x Time	Saline/cryo	Post	Saline/sham	Post	3.03	72	.002
Cond x Time	Saline/cryo	Post	Saline/sham	30 post	1.08	72	.003
Cond x Time	Saline/cryo	Post	No saline	Pre	1.11	72	.28
Cond x Time	Saline/cryo	Post	No saline	Post	1.02	72	.27
Cond x Time	Saline/cryo	Post	No saline	30 post	0.31	72	.31
Cond x Time	Saline/cryo	30 post	Saline/sham	Pre	1.81	72	.76
Cond x Time	Saline/cryo	30 post	Saline/sham	Post	1.53	72	.07
Cond x Time	Saline/cryo	30 post	Saline/sham	30 post	-0.42	72	.13
Cond x Time	Saline/cryo	30 post	No saline	Pre	-0.39	72	.68
Cond x Time	Saline/cryo	30 post	No saline	Post	-0.49	72	.70
Cond x Time	Saline/cryo	30 post	No saline	30 post	4.31	72	.63

Table C 17. Continued

Cond x Time	Saline/sham	Pre	Saline/sham	Post	3.50	72	<.0001*
Cond x Time	Saline/sham	Pre	Saline/sham	30 post	-0.73	72	.0008*
Cond x Time	Saline/sham	Pre	No saline	Pre	-0.70	72	.47
Cond x Time	Saline/sham	Pre	No saline	Post	-0.80	72	.49
Cond x Time	Saline/sham	Pre	No saline	30 post	-0.81	72	.43
Cond x Time	Saline/sham	Post	Saline/sham	30 post	-2.22	72	.42
Cond x Time	Saline/sham	Post	No saline	Pre	-2.19	72	.03*
Cond x Time	Saline/sham	Post	No saline	Post	-2.29	72	.03*
Cond x Time	Saline/sham	Post	No saline	30 post	-1.94	72	.02*
Cond x Time	Saline/sham	30 post	No saline	Pre	-1.91	72	.06
Cond x Time	Saline/sham	30 post	No saline	Post	-2.01	72	.06
Cond x Time	Saline/sham	30 post	No saline	30 post	0.09	72	.05
Cond x Time	No saline	Pre	No saline	Post	-0.20	72	.93
Cond x Time	No saline	Pre	No saline	30 post	-0.29	72	.85
Cond x Time	No saline	Post	No saline	30 post	3.58	72	.78

* = represents a significant difference

Table C 18. M_{max} Measure for Each Condition Across Time. Measures were Taken Before, Immediately After, and 30 minutes Following Each of the 4 Conditions (n = 3 Measures/Condition; Mean ± SD)

Condition	Pre	$Post_{tx}$	30 min $post_{tx}$
Saline	7.3 ± 1.7	7.1 ± 1.8	7.2 ± 1.8
Saline/cryo	7.6 ± 1.0	7.6 ± 1.1	7.7 ± 0.9
Saline/sham	7.3 ± 1.2	7.1 ± 1.4	7.2 ± 1.4
No saline	7.3 ± 1.9	7.3 ± 1.9	7.3 ± 1.9

Table C 19. Mixed Model Procedures for Fixed Effects Differences Between Condition and Time for the M_{max}

Effect	Numerator Degrees of Freedom	Denominator Degrees of Freedom	F-value	*P*-value
Time	2	72	1.6	.20
Condition	3	72	0.2	.93
Cond x Time	6	72	1.0	.46

Table C 20. Least Means Squares Differences for the M_{max}

Effect	Cond	Time	Cond	Time	t-value	DF	*P*-value
Cond x Time	Saline	Pre	Saline	Post	1.60	72	.11
Cond x Time	Saline	Pre	Saline	30 post	1.52	72	.13
Cond x Time	Saline	Pre	Saline	Pre	-0.38	72	.70
Cond x Time	Saline	Pre	Saline/cryo	Post	-0.45	72	.65
Cond x Time	Saline	Pre	Saline/cryo	30 post	-0.51	72	.61
Cond x Time	Saline	Pre	Saline/cryo	Pre	-0.05	72	.96
Cond x Time	Saline	Pre	Saline/sham	Post	0.27	72	.79
Cond x Time	Saline	Pre	Saline/sham	30 post	0.12	72	.90
Cond x Time	Saline	Pre	Saline/sham	Pre	0.01	72	.99
Cond x Time	Saline	Pre	No saline	Post	0.05	72	.96
Cond x Time	Saline	Pre	No saline	30 post	-0.05	72	.96
Cond x Time	Saline	Post	No saline	30 post	-0.08	72	.94
Cond x Time	Saline	Post	Saline	Pre	-0.62	72	.54
Cond x Time	Saline	Post	Saline/cryo	Post	-0.69	72	.49
Cond x Time	Saline	Post	Saline/cryo	30 post	-0.75	72	.46
Cond x Time	Saline	Post	Saline/cryo	Pre	-0.29	72	.77
Cond x Time	Saline	Post	Saline/sham	Post	0.03	72	.98
Cond x Time	Saline	Post	Saline/sham	30 post	-0.12	72	.91
Cond x Time	Saline	Post	Saline/sham	Pre	-0.23	72	.82
Cond x Time	Saline	Post	No saline	Post	-0.18	72	.85
Cond x Time	Saline	Post	No saline	30 post	-0.29	72	.77
Cond x Time	Saline	30 post	No saline	Pre	-0.61	72	.54
Cond x Time	Saline	30 post	Saline/cryo	Post	-0.68	72	.50
Cond x Time	Saline	30 post	Saline/cryo	30 post	-0.74	72	.46
Cond x Time	Saline	30 post	Saline/cryo	Pre	-0.28	72	.78
Cond x Time	Saline	30 post	Saline/sham	Post	0.04	72	.97
Cond x Time	Saline	30 post	Saline/sham	30 post	-0.11	72	.92
Cond x Time	Saline	30 post	Saline/sham	Pre	-0.22	72	.83
Cond x Time	Saline	30 post	No saline	Post	-0.17	72	.86
Cond x Time	Saline	30 post	No saline	30 post	-0.28	72	.78
Cond x Time	Saline/cryo	Pre	No saline	Post	-0.45	72	.65
Cond x Time	Saline/cryo	Pre	Saline/cryo	30 post	-0.85	72	.40
Cond x Time	Saline/cryo	Pre	Saline/cryo	Pre	0.33	72	.74
Cond x Time	Saline/cryo	Pre	Saline/sham	Post	0.65	72	.52
Cond x Time	Saline/cryo	Pre	Saline/sham	30 post	0.51	72	.61
Cond x Time	Saline/cryo	Pre	Saline/sham	Pre	0.39	72	.70
Cond x Time	Saline/cryo	Pre	No saline	Post	0.44	72	.66
Cond x Time	Saline/cryo	Pre	No saline	30 post	0.33	72	.74
Cond x Time	Saline/cryo	Post	No saline	30 post	-0.40	72	.69
Cond x Time	Saline/cryo	Post	Saline/cryo	Pre	0.40	72	.69
Cond x Time	Saline/cryo	Post	Saline/sham	Post	0.72	72	.48
Cond x Time	Saline/cryo	Post	Saline/sham	30 post	0.57	72	.57
Cond x Time	Saline/cryo	Post	Saline/sham	Pre	0.46	72	.65
Cond x Time	Saline/cryo	Post	No saline	Post	0.51	72	.61
Cond x Time	Saline/cryo	Post	No saline	30 post	0.40	72	.69
Cond x Time	Saline/cryo	30 post	No saline	Pre	0.46	72	.65
Cond x Time	Saline/cryo	30 post	Saline/sham	Post	0.78	72	.44
Cond x Time	Saline/cryo	30 post	Saline/sham	30 post	0.63	72	.53
Cond x Time	Saline/cryo	30 post	Saline/sham	Pre	0.52	72	.61
Cond x Time	Saline/cryo	30 post	No saline	Post	0.57	72	.57
Cond x Time	Saline/cryo	30 post	No saline	30 post	0.46	72	.65

Table C 20. Continued

Cond x Time	Saline/sham	Pre	No saline	Post	2.13	72	.04*
Cond x Time	Saline/sham	Pre	Saline/sham	30 post	1.18	72	.24
Cond x Time	Saline/sham	Pre	Saline/sham	Pre	0.06	72	.95
Cond x Time	Saline/sham	Pre	No saline	Post	0.11	72	.91
Cond x Time	Saline/sham	Pre	No saline	30 post	0.00	72	1.00
Cond x Time	Saline/sham	Post	No saline	30 post	-0.95	72	.35
Cond x Time	Saline/sham	Post	Saline/sham	Pre	-0.26	72	.80
Cond x Time	Saline/sham	Post	No saline	Post	-0.21	72	.83
Cond x Time	Saline/sham	Post	No saline	30 post	-0.32	72	.75
Cond x Time	Saline/sham	30 post	No saline	Pre	-0.11	72	.91
Cond x Time	Saline/sham	30 post	No saline	Post	-0.07	72	.95
Cond x Time	Saline/sham	30 post	No saline	30 post	-0.17	72	.86
Cond x Time	No saline	Pre	No saline	Post	0.31	72	.76
Cond x Time	No saline	Pre	No saline	30 post	-0.39	72	.69
Cond x Time	No saline	Post	No saline	30 post	-0.70	72	.48

Table C 21. H:M_{max} Ratios for Conditions Across Time. Measures were Taken Before, Immediately After, and 30 Minutes Following Each of the 4 Conditions (n = 3 Measures/Condition; Mean ± SD)

Condition	Pre	$Post_{tx}$‡	30 min $post_{tx}$‡
Saline*	0.4 ± 0.2	0.3 ± 0.2	0.3 ± 0.2
Saline/cryo†	0.4 ± 0.1	0.6 ± 0.2	0.4 ± 0.2
Saline/sham*	0.4 ± 0.2	0.2 ± 0.2	0.3 ± 0.2
No saline	0.4 ± 0.2	0.5 ± 0.2	0.5 ± 0.2

*Pre > $post_{tx}$ and 30 min $post_{tx}$

†$Post_{tx}$ > pre and 30 min $post_{tx}$

‡Saline/cryo > saline and saline/sham

§No saline > saline and saline/sham

Table C 22. Mixed Model Procedures for Fixed Effects Differences Between Condition and Time for the H:M_{max} Ratios

Effect	Numerator Degrees of Freedom	Denominator Degrees of Freedom	F-value	*P*-value
Time	2	72	7.5	.001*
Condition	3	72	1.6	.2
Cond x Time	6	72	13.1	<.0001*

* = represents a significant difference

Table C 23. Least Square Means Differences Between Condition and Time for the $H:M_{max}$ Ratio

Effect	Condition	Time	Condition	Time	DF	t-value	*P*-value
Cond x Time	Saline	Pre	Saline	Post	72	4.58	<.0001*
Cond x Time	Saline	Pre	Saline	30 post	72	3.88	.0002*
Cond x Time	Saline	Pre	Saline/cryo	Pre	72	0.46	.65
Cond x Time	Saline	Pre	Saline/cryo	Post	72	-1.57	.12
Cond x Time	Saline	Pre	Saline/cryo	30 post	72	0.52	.61
Cond x Time	Saline	Pre	Saline/sham	Pre	72	0.26	.80
Cond x Time	Saline	Pre	Saline/sham	Post	72	1.90	.06
Cond x Time	Saline	Pre	Saline/sham	30 post	72	1.65	.10
Cond x Time	Saline	Pre	No saline	Pre	72	-0.39	.70
Cond x Time	Saline	Pre	No saline	Post	72	-0.46	.65
Cond x Time	Saline	Pre	No saline	30 post	72	-0.48	.63
Cond x Time	Saline	Post	Saline	30 post	72	-0.70	.49
Cond x Time	Saline	Post	Saline/cryo	Pre	72	-1.17	.24
Cond x Time	Saline	Post	Saline/cryo	Post	72	-3.20	.002*
Cond x Time	Saline	Post	Saline/cryo	30 post	72	-1.11	.27
Cond x Time	Saline	Post	Saline/sham	Pre	72	-1.37	.17
Cond x Time	Saline	Post	Saline/sham	Post	72	0.27	.79
Cond x Time	Saline	Post	Saline/sham	30 post	72	0.02	.98
Cond x Time	Saline	Post	No saline	Pre	72	-2.02	.05
Cond x Time	Saline	Post	No saline	Post	72	-2.09	.04*
Cond x Time	Saline	Post	No saline	30 post	72	-2.11	.04*
Cond x Time	Saline	30 post	Saline/cryo	Pre	72	-0.92	.36
Cond x Time	Saline	30 post	Saline/cryo	Post	72	-2.95	.004*
Cond x Time	Saline	30 post	Saline/cryo	30 post	72	-0.87	.39
Cond x Time	Saline	30 post	Saline/sham	Pre	72	-1.13	.26
Cond x Time	Saline	30 post	Saline/sham	Post	72	0.52	.60
Cond x Time	Saline	30 post	Saline/sham	30 post	72	0.27	.79
Cond x Time	Saline	30 post	No saline	Pre	72	-1.77	.08
Cond x Time	Saline	30 post	No saline	Post	72	-1.84	.07
Cond x Time	Saline	30 post	No saline	30 post	72	-1.87	.04*
Cond x Time	Saline/cryo	Pre	Saline/cryo	Post	72	-5.68	<.0001*
Cond x Time	Saline/cryo	Pre	Saline/cryo	30 post	72	0.16	.87
Cond x Time	Saline/cryo	Pre	Saline/sham	Pre	72	-0.20	.84
Cond x Time	Saline/cryo	Pre	Saline/sham	Post	72	1.45	.15
Cond x Time	Saline/cryo	Pre	Saline/sham	30 post	72	1.20	.24
Cond x Time	Saline/cryo	Pre	No saline	Pre	72	-0.84	.40
Cond x Time	Saline/cryo	Pre	No saline	Post	72	-0.92	.36
Cond x Time	Saline/cryo	Pre	No saline	30 post	72	-0.94	.35
Cond x Time	Saline/cryo	Post	Saline/cryo	30 post	72	5.85	<.0001*
Cond x Time	Saline/cryo	Post	Saline/sham	Pre	72	1.82	.07
Cond x Time	Saline/cryo	Post	Saline/sham	Post	72	3.47	.0009*
Cond x Time	Saline/cryo	Post	Saline/sham	30 post	72	3.22	.002*
Cond x Time	Saline/cryo	Post	No saline	Pre	72	1.18	.24
Cond x Time	Saline/cryo	Post	No saline	Post	72	1.10	.27
Cond x Time	Saline/cryo	Post	No saline	30 post	72	1.08	.28
Cond x Time	Saline/cryo	30 post	Saline/sham	Pre	72	-0.26	.80
Cond x Time	Saline/cryo	30 post	Saline/sham	Post	72	1.39	.17
Cond x Time	Saline/cryo	30 post	Saline/sham	30 post	72	1.14	.26
Cond x Time	Saline/cryo	30 post	No saline	Pre	72	-0.90	.37
Cond x Time	Saline/cryo	30 post	No saline	Post	72	-0.98	.33

Table C 23. Continued

Cond x Time	Saline/cryo	30 post	No saline	30 post	72	-1.00	.32
Cond x Time	Saline/sham	Pre	Saline/sham	Post	72	4.63	<.0001*
Cond x Time	Saline/sham	Pre	Saline/sham	30 post	72	3.93	.0002*
Cond x Time	Saline/sham	Pre	No saline	Pre	72	-0.64	.52
Cond x Time	Saline/sham	Pre	No saline	Post	72	-0.72	.48
Cond x Time	Saline/sham	Pre	No saline	30 post	72	-0.74	.46
Cond x Time	Saline/sham	Post	Saline/sham	30 post	72	-0.70	.49
Cond x Time	Saline/sham	Post	No saline	Pre	72	-2.29	.03*
Cond x Time	Saline/sham	Post	No saline	Post	72	-2.36	.02*
Cond x Time	Saline/sham	Post	No saline	30 post	72	-2.39	.02*
Cond x Time	Saline/sham	30 post	No saline	Pre	72	-2.04	.04*
Cond x Time	Saline/sham	30 post	No saline	Post	72	-2.12	.05
Cond x Time	Saline/sham	30 post	No saline	30 post	72	-2.14	.03*
Cond x Time	No saline	Pre	No saline	Post	72	-0.21	.84
Cond x Time	No saline	Pre	No saline	30 post	72	-0.27	.79
Cond x Time	No saline	Post	No saline	30 post	72	-0.07	.95

* = represents a significant difference

Table C 24. Percent Change in H:M_{max} Ratio Over Time. Data are Presented as Percent Change from Preinfusion (± SD). Percentages Less Than 0 Indicates Quadriceps Motoneuron Pool Facilitation; Values Less Than 0 Indicates Quadriceps AMI

	Pre	$Post_{tx}$	30 min $post_{tx}$
Saline	0 ± 0	-37.0 ± 17.3	-31.2 ± 10.8
Saline/cryo	0 ± 0	50.9 ± 41.3	-1.5 ± 46.5
Saline/sham	0 ± 0	-39.5 ± 8.2	-33.5 ± 13.7
No saline	0 ± 0	1.5 ± -1.5	2.0 ± -2.1

Table C 25. Calculated PRI for Conditions Across Time. Measures Include the Average Value for the Sensory, Affective, Evaluative, and Miscellaneous Sections of MPQ (n = 3 Measures/Condition; Mean ± SD)

Condition	Pre	$Post_{tx}$ ‡	30 min $post_{tx}$ §
Saline*	0.0 ± 0.0	17.1 ± 10.3	5.3 ± 6.2
Saline/cryo†	0.0 ± 0.0	12.2 ± 4.2	8.2 ± 8.2
Saline/sham*	0.0 ± 0.0	16.0 ± 7.7	5.1 ± 4.7
No saline	0.1 ± 0.3	0.7 ± 1.1	0.4 ± 0.7

*$Post_{tx}$ > 30 min $post_{tx}$ & pre; 30 min $post_{tx}$ > pre

†$Post_{tx}$ and 30 min $post_{tx}$ > pre

‡Saline, saline/cryo, and saline/sham > no-saline

§Saline/cryo > no-saline

Table C 26. Mixed Model Procedures for Fixed Effects Differences Between Condition and Time as Calculated with the PRI

Effect	Numerator Degrees of Freedom	Denominator Degrees of Freedom	F-Value	*P*-value
Time	1	36	36.3	<.0001*
Condition	3	36	9.7	<.0001*
Cond x Time	3	36	6.1	.002*

* = represents a significant difference

Table C 27. Least Square Means Between Condition and Time for the PRI

Effect	Condition	Time	DF	Effect	*P*-value
Cond x Time	Saline	Post	36	8.64	<.0001*
Cond x Time	Saline	30 post	36	2.68	.01*
Cond x Time	Saline/cryo	Post	36	6.16	<.0001*
Cond x Time	Saline/cryo	30 post	36	4.14	.0002*
Cond x Time	Saline/sham	Post	36	8.09	<.0001*
Cond x Time	Saline/sham	30 post	36	2.58	.01*
Cond x Time	No saline	Post	36	0.35	.73
Cond x Time	No saline	30 post	36	0.20	.84

* = represents a significant difference

Table C 28. Least Square Means Differences Between Condition and Time for the PRI

Effect	Cond	Time	Cond	Time	DF	t-value	*P*-value
Cond x Time	Saline	Post	Saline	30 post	36	5.27	<.0001*
Cond x Time	Saline	Post	Saline/cryo	Post	36	1.75	.09
Cond x Time	Saline	Post	Saline/cryo	30 post	36	3.18	.003*
Cond x Time	Saline	Post	Saline/sham	Post	36	0.39	.70
Cond x Time	Saline	Post	Saline/sham	30 post	36	4.29	.0001*
Cond x Time	Saline	Post	No saline	Post	36	5.86	<.0001*
Cond x Time	Saline	Post	No saline	30 post	36	5.97	<.0001*
Cond x Time	Saline	30 post	Saline/cryo	Post	36	-2.47	.02*
Cond x Time	Saline	30 post	Saline/cryo	30 post	36	-1.04	.31
Cond x Time	Saline	30 post	Saline/sham	Post	36	-3.82	.0005*
Cond x Time	Saline	30 post	Saline/sham	30 post	36	0.07	.94
Cond x Time	Saline	30 post	No saline	Post	36	1.64	.11
Cond x Time	Saline	30 post	No saline	30 post	36	1.75	.09
Cond x Time	Saline/cryo	Post	Saline/cryo	30 post	36	1.79	.08
Cond x Time	Saline/cryo	Post	Saline/sham	Post	36	-1.36	.18
Cond x Time	Saline/cryo	Post	Saline/sham	30 post	36	2.54	.02*
Cond x Time	Saline/cryo	Post	No saline	Post	36	4.11	.0002*
Cond x Time	Saline/cryo	Post	No saline	30 post	36	4.22	.0002*
Cond x Time	Saline/cryo	30 post	Saline/sham	Post	36	-2.79	.008*
Cond x Time	Saline/cryo	30 post	Saline/sham	30 post	36	1.11	.28
Cond x Time	Saline/cryo	30 post	No saline	Post	36	2.68	.01*
Cond x Time	Saline/cryo	30 post	No saline	30 post	36	2.79	.008*
Cond x Time	Saline/sham	Post	Saline/sham	30 post	36	4.87	<.0001*
Cond x Time	Saline/sham	Post	No saline	Post	36	5.47	<.0001*
Cond x Time	Saline/sham	Post	No saline	30 post	36	5.57	<.0001*
Cond x Time	Saline/sham	30 post	No saline	Post	36	1.57	.12
Cond x Time	Saline/sham	30 post	No saline	30 post	36	1.68	.10
Cond x Time	No saline	Post	No saline	30 post	36	0.13	.89

* = represents a significant difference

Table C 29. Pain Perception as Measured on each VAS (n = 3 Measures/Condition; Mean ± SD)

Condition	Pre	$Post_{tx}$ [†]	30 min $post_{tx}$ [‡]
Saline[*]	0.0 ± 0.0	49.5 ± 23.7	8.4 ± 9.5
Saline/cryo[*]	0.0 ± 0.0	28.6 ± 7.7	12.1 ± 8.0
Saline/sham[*]	0.0 ± 0.0	45.5 ± 24.3	13.8 ± 13.8
No saline	0.0 ± 0.0	0.7 ± 1.3	0.5 ± 0.9[‡]

[*] $Post_{tx}$ > 30 min $post_{tx}$ & pre; 30 min $post_{tx}$ > pre
[†] Saline & saline/sham > saline/cryo > no-saline
[‡] Saline/cryo & saline/sham > no-saline

Table C 30. Mixed Model Procedures for Fixed Effects Differences Between Condition and Time for Pain Perception as Measured on the VAS

Effect	Numerator Degrees of Freedom	Denominator Degrees of Freedom	F-Value	*P*-value
Time	1	36	86.31	<.0001[*]
Cond	3	36	13.41	<.0001[*]
Cond x Time	3	36	13.85	<.0001[*]

[*] = represents a significant difference

Table C 31. Least Square Means Between Condition and Time for Pain Perception as Measured on the VAS

Effect	Condition	Time	DF	t-value	*P*-value
Cond x Time	Saline	Post	36	11.22	<.0001[*]
Cond x Time	Saline	30 post	36	1.90	.04[*]
Cond x Time	Saline/cryo	Post	36	6.48	<.0001[*]
Cond x Time	Saline/cryo	30 post	36	2.74	.009[*]
Cond x Time	Saline/sham	Post	36	10.31	<.0001[*]
Cond x Time	Saline/sham	30 post	36	3.13	.004[*]
Cond x Time	No saline	Post	36	0.16	.87
Cond x Time	No saline	30 post	36	0.11	.91

[*] = represents a significant difference

Table C 32. Least Square Means Differences Between Condition and Time for Pain Perception as Measured on the VAS

Effect	Condition	Time	Condition	Time	DF	t-value	*P*-value
Cond x Time	Saline	Post	Saline	30 post	36	8.53	<.0001*
Cond x Time	Saline	Post	Saline/cryo	Post	36	3.35	.002*
Cond x Time	Saline	Post	Saline/cryo	30 post	36	5.99	<.0001*
Cond x Time	Saline	Post	Saline/sham	Post	36	0.64	.53
Cond x Time	Saline	Post	Saline/sham	30 post	36	5.72	<.0001*
Cond x Time	Saline	Post	No saline	Post	36	7.82	<.0001*
Cond x Time	Saline	Post	No saline	30 post	36	7.85	<.0001*
Cond x Time	Saline	30 post	Saline/cryo	Post	36	-3.24	.003*
Cond x Time	Saline	30 post	Saline/cryo	30 post	36	-0.59	.55
Cond x Time	Saline	30 post	Saline/sham	Post	36	-5.95	<.0001*
Cond x Time	Saline	30 post	Saline/sham	30 post	36	-0.87	.39
Cond x Time	Saline	30 post	No saline	Post	36	1.23	.23
Cond x Time	Saline	30 post	No saline	30 post	36	1.27	.21
Cond x Time	Saline/cryo	Post	Saline/cryo	30 post	36	3.43	.002*
Cond x Time	Saline/cryo	Post	Saline/sham	Post	36	2.71	.01*
Cond x Time	Saline/cryo	Post	Saline/sham	30 Post	36	2.37	.02*
Cond x Time	Saline/cryo	Post	No saline	30 post	36	4.47	<.0001*
Cond x Time	Saline/cryo	Post	No saline	Post	36	4.50	<.0001*
Cond x Time	Saline/cryo	30 post	Saline/sham	Post	36	-5.35	<.0001*
Cond x Time	Saline/cryo	30 post	Saline/sham	30 post	36	-0.27	.79
Cond x Time	Saline/cryo	30 post	No saline	30 post	36	1.83	.04*
Cond x Time	Saline/cryo	30 post	No saline	Post	36	1.86	.04*
Cond x Time	Saline/sham	Post	Saline/sham	30 post	36	6.58	<.0001*
Cond x Time	Saline/sham	Post	No saline	30 post	36	7.18	<.0001*
Cond x Time	Saline/sham	Post	No saline	Post	36	7.21	<.0001*
Cond x Time	Saline/sham	30 post	No saline	30 post	36	2.10	.03*
Cond x Time	Saline/sham	30 post	No saline	Post	36	2.13	.03*
Cond x Time	No saline	Post	No saline	30 post	36	0.04	.97

* = represents a significant difference

Table C 33. PPI for Conditions Across Time (n = 3 Measures/Condition; Mean ± SD)

Condition	Pre	$Post_{tx}$†	30 min $post_{tx}$‡
Saline*	0.0 ± 0.0	2.2 ± 0.6	0.8 ± 0.6
Saline/cryo*	0.0 ± 0.0	3.8 ± 5.7	1.0 ± 0.7
Saline/sham*	0.0 ± 0.0	2.4 ± 0.8	1.0 ± 0.8
No saline	0.0 ± 0.0	0.1 ± 3.2	0.2 ± 0.4

*$Post_{tx}$ > 30 min $post_{tx}$ and pre. 30 min $post_{tx}$ > pre

†No saline < saline, saline/cryo, and saline/sham

‡No saline < saline, saline/cryo, and saline/sham

Table C 34. Mixed Model Procedures for Fixed Effects Differences Between Condition and Time for the PPI

Effect	Numerator Degrees of Freedom	Denominator Degrees of Freedom	F-Value	*P*-value
Time	1	36	69.6	<.0001*
Cond	3	36	19.1	<.0001*
Cond x Time	3	36	10.2	<.0001*

* = represents a significant difference

Table C 35. Least Square Means Between Condition and Time for the PPI

Effect	Cond	Time	DF	t-value	*P*-value
Cond x Time	Saline	Post	36	11.14	<.0001*
Cond x Time	Saline	30 post	36	4.05	.0003*
Cond x Time	Saline/cryo	Post	36	10.12	<.0001*
Cond x Time	Saline/cryo	30 post	36	5.06	<.0001*
Cond x Time	Saline/sham	Post	36	12.15	<.0001*
Cond x Time	Saline/sham	30 post	36	5.06	<.0001*
Cond x Time	No saline	Post	36	0.51	.62
Cond x Time	No saline	30 post	36	1.01	.32

* = represents a significant difference

Table C 36. Least Square Means Differences Between Condition and Time for the PPI

Effect	Cond	Time	Cond	Time	DF	t-value	*P*-value
Cond x Time	Saline	Post	Saline	30 post	36	6.31	<.0001*
Cond x Time	Saline	Post	Saline/cryo	Post	36	0.72	1.0
Cond x Time	Saline	Post	Saline/cryo	30 post	36	4.30	.003*
Cond x Time	Saline	Post	Saline/sham	Post	36	-0.72	1.0
Cond x Time	Saline	Post	Saline/sham	30 post	36	4.30	.003*
Cond x Time	Saline	Post	No saline	Post	36	7.52	<.0001*
Cond x Time	Saline	Post	No saline	30 post	36	7.16	<.0001*
Cond x Time	Saline	30 post	Saline/cryo	Post	36	-4.30	.003*
Cond x Time	Saline	30 post	Saline/cryo	30 post	36	-0.72	1.0
Cond x Time	Saline	30 post	Saline/sham	Post	36	-5.73	<.0001*
Cond x Time	Saline	30 post	Saline/sham	30 post	36	-0.72	1.0
Cond x Time	Saline	30 post	No saline	Post	36	2.51	.23
Cond x Time	Saline	30 post	No saline	30 post	36	2.15	.41
Cond x Time	Saline/cryo	Post	Saline/cryo	30 post	36	4.51	.002*
Cond x Time	Saline/cryo	Post	Saline/sham	Post	36	-1.43	.84
Cond x Time	Saline/cryo	Post	Saline/sham	30 post	36	3.58	.02*
Cond x Time	Saline/cryo	Post	No saline	Post	36	6.80	<.0001*
Cond x Time	Saline/cryo	Post	No saline	30 post	36	6.44	<.0001*
Cond x Time	Saline/cryo	30 post	Saline/sham	Post	36	-5.01	.0004*
Cond x Time	Saline/cryo	30 post	Saline/sham	30 post	36	0.00	1.0
Cond x Time	Saline/cryo	30 post	No saline	Post	36	3.22	.05
Cond x Time	Saline/cryo	30 post	No saline	30 post	36	2.86	.11
Cond x Time	Saline/sham	Post	Saline/sham	30 post	36	6.31	<.0001*
Cond x Time	Saline/sham	Post	No saline	Post	36	8.23	<.0001*
Cond x Time	Saline/sham	Post	No saline	30 post	36	7.87	<.0001*
Cond x Time	Saline/sham	30 post	No saline	Post	36	3.22	.05
Cond x Time	Saline/sham	30 post	No saline	30 post	36	2.86	.11
Cond x Time	No saline	Post	No saline	30 post	36	-0.45	1.0

* = represents a significant difference

Table C 37. Popliteal Surface Temperature (°C) for each Condition. Measures were Taken at the Last Minute During the 3 Application Phases (n = 3 Measures/Condition; Mean ± SD)

Condition	Pre	$Post_{tx}$ †	30 min $post_{tx}$ †
Saline	33.2 ± 0.7	30.5 ± 1.1	33.5 ± 1.6
Saline/cryo*	32.7 ± 0.9	6.9 ± 2.9	28.2 ± 1.7
Saline/sham	32.4 ± 1.0	32.4 ± 1.4	33.4 ± 0.9
No saline	32.3 ± 1.1	33.6 ± 1.1	33.6 ± 1.0

*$Post_{tx}$ < 30 min $post_{tx}$ & pre; 30 min $post_{tx}$ < pre

†Saline/cryo < saline, saline/sham, & no-saline

Table C 38. Mixed Model Procedures for Fixed Effects Differences Between Condition and Time for Popliteal Surface Temperature

Effect	Numerator Degrees of Freedom	Denominator Degrees of Freedom	F-value	*P*-Value
Time	2	72	317.9	<.0001*
Cond	3	72	274.2	<.0001*
Cond x Time	6	72	343.2	<.0001*

* = represents a significant difference

Table C 39. Least Square Means Differences Between Condition and Time for the Popliteal Surface Temperature

Effect	Cond	Time	Cond	Time	DF	t-value	*P*-value
Cond x Time	Saline	0	Saline	20	72	-0.63	1.0
Cond x Time	Saline	0	Saline	50	72	-0.58	1.0
Cond x Time	Saline	0	Saline/cryo	0	72	0.84	1.0
Cond x Time	Saline	0	Saline/cryo	20	72	42.05	<.0001*
Cond x Time	Saline	0	Saline/cryo	50	72	7.97	<.0001*
Cond x Time	Saline	0	Saline/sham	0	72	1.28	.98
Cond x Time	Saline	0	Saline/sham	20	72	1.19	.99
Cond x Time	Saline	0	Saline/sham	50	72	-0.35	1.0
Cond x Time	Saline	0	No saline	0	72	1.43	.95
Cond x Time	Saline	0	No saline	20	72	-0.65	1.0
Cond x Time	Saline	0	No saline	50	72	-0.70	1.0
Cond x Time	Saline	20	Saline	50	72	0.06	1.0
Cond x Time	Saline	20	Saline/cryo	0	72	1.38	.96
Cond x Time	Saline	20	Saline/cryo	20	72	42.59	<.0001*
Cond x Time	Saline	20	Saline/cryo	50	72	8.51	<.0001*
Cond x Time	Saline	20	Saline/sham	0	72	1.82	.80
Cond x Time	Saline	20	Saline/sham	20	72	1.73	.85
Cond x Time	Saline	20	Saline/sham	50	72	0.19	1.0
Cond x Time	Saline	20	No saline	0	72	1.97	.71
Cond x Time	Saline	20	No saline	20	72	-0.11	1.0
Cond x Time	Saline	20	No saline	50	72	-0.16	1.0
Cond x Time	Saline	50	Saline/cryo	0	72	1.33	.97
Cond x Time	Saline	50	Saline/cryo	20	72	42.54	<.0001*
Cond x Time	Saline	50	Saline/cryo	50	72	8.46	<.0001*
Cond x Time	Saline	50	Saline/sham	0	72	1.77	.83
Cond x Time	Saline	50	Saline/sham	20	72	1.68	.87
Cond x Time	Saline	50	Saline/sham	50	72	0.14	1.0
Cond x Time	Saline	50	No saline	0	72	1.92	.75
Cond x Time	Saline	50	No saline	20	72	-0.16	1.0
Cond x Time	Saline	50	No saline	50	72	-0.21	1.0
Cond x Time	Saline/cryo	0	Saline/cryo	20	72	48.45	<.0001*
Cond x Time	Saline/cryo	0	Saline/cryo	50	72	8.38	<.0001*
Cond x Time	Saline/cryo	0	Saline/sham	0	72	0.44	1.0
Cond x Time	Saline/cryo	0	Saline/Sham	20	72	0.35	1.0
Cond x Time	Saline/cryo	0	Saline/Sham	50	72	-1.19	.99
Cond x Time	Saline/cryo	0	No saline	0	72	0.59	1.0
Cond x Time	Saline/cryo	0	No saline	20	72	-1.49	.94
Cond x Time	Saline/cryo	0	No saline	50	72	-1.54	.92
Cond x Time	Saline/cryo	20	Saline/cryo	50	72	-40.07	<.0001*
Cond x Time	Saline/cryo	20	Saline/sham	0	72	-40.78	<.0001*
Cond x Time	Saline/cryo	20	Saline/Sham	20	72	-40.87	<.0001*
Cond x Time	Saline/cryo	20	Saline/Sham	50	72	-42.41	<.0001*
Cond x Time	Saline/cryo	20	No saline	0	72	-40.63	<.0001*
Cond x Time	Saline/cryo	20	No saline	20	72	-42.70	<.0001*
Cond x Time	Saline/cryo	20	No saline	50	72	-42.76	<.0001*
Cond x Time	Saline/cryo	50	Saline/sham	0	72	-6.69	<.0001*
Cond x Time	Saline/cryo	50	Saline/sham	20	72	-6.78	<.0001*
Cond x Time	Saline/cryo	50	Saline/sham	50	72	-8.32	<.0001*
Cond x Time	Saline/cryo	50	No saline	0	72	-6.54	<.0001*
Cond x Time	Saline/cryo	50	No saline	20	72	-8.61	<.0001*

Table C 39. Continued

Cond x Time	Saline/cryo	50	No saline	50	72	-8.67	<.0001*
Cond x Time	Saline/sham	0	Saline/sham	20	72	-0.11	1.0
Cond x Time	Saline/sham	0	Saline/sham	50	72	-1.92	.74
Cond x Time	Saline/sham	0	No saline	0	72	0.15	1.0
Cond x Time	Saline/sham	0	No saline	20	72	-1.92	.74
Cond x Time	Saline/sham	0	No saline	50	72	-1.98	.70
Cond x Time	Saline/sham	20	Saline/sham	50	72	-1.81	.81
Cond x Time	Saline/sham	20	No saline	0	72	0.24	1.0
Cond x Time	Saline/sham	20	No saline	20	72	-1.83	.79
Cond x Time	Saline/sham	20	No saline	50	72	-1.89	.76
Cond x Time	Saline/sham	50	No saline	0	72	1.78	.82
Cond x Time	Saline/sham	50	No saline	20	72	-0.29	1.0
Cond x Time	Saline/sham	50	No saline	50	72	-0.35	1.0
Cond x Time	No saline	0	No saline	20	72	-2.44	.40
Cond x Time	No saline	0	No saline	50	72	-2.50	.35
Cond x Time	No saline	20	No saline	50	72	-0.07	1.0

* = represents a significant difference
0 = pre
20 = $post_{tx}$
50 = 30 min $post_{tx}$

Table C 40. Patella Surface Temperature (°C) for each Condition. Measures were Taken at the Last Minute During the 3 Application Phases (n = 3 measures/condition: mean ± SD)

Condition	Pre	$Post_{tx}$†	30 min $post_{tx}$†
Saline	28.2 ± 1.1	28.1 ± 1.0	28.2 ± 1.1
Saline/cryo*	27.1 ± 1.9	10.5 ± 4.5	16.3 ± 4.0
Saline/sham	28.0 ± 0.9	27.9 ± 0.9	28.3 ± 1.2
No saline	27.3 ± 1.0	27.5 ± 0.8	27.4 ± 0.5

*$Post_{tx}$ < 30 min $post_{tx}$ & pre; 30 min $post_{tx}$ < pre
†Saline/cryo < saline, saline/sham, & no-saline

Table C 41. Mixed Model Procedures for Fixed Effects Differences Between Condition and Time for Patella Surface Temperature

Effect	Numerator Degrees of Freedom	Denominator Degrees of Freedom	F-value	*P*-value
Time	2	72	215.0	<.0001*
Cond	3	72	151.1	<.0001*
Cond x Time	6	72	205.9	<.0001*

* = represents a significant difference

Table C 42. Least Square Means Differences Between Condition and Time for Patella Surface Temperature

Effect	Condition	Time	Condition	Time	DF	t- value	*P*-value
Cond x Time	Saline	0	Saline	20	72	0.54	1.0
Cond x Time	Saline	0	Saline	50	72	-0.52	1.0
Cond x Time	Saline	0	Saline/cryo	0	72	0.82	1.0
Cond x Time	Saline	0	Saline/cryo	20	72	30.54	<.0001*
Cond x Time	Saline	0	Saline/cryo	50	72	11.52	<.0001*
Cond x Time	Saline	0	Saline/sham	0	72	0.50	1.0
Cond x Time	Saline	0	Saline/sham	20	72	0.45	1.0
Cond x Time	Saline	0	Saline/sham	50	72	-0.52	1.0
Cond x Time	Saline	0	No saline	0	72	1.35	.97
Cond x Time	Saline	0	No saline	20	72	1.20	.99
Cond x Time	Saline	0	No saline	50	72	1.30	.98
Cond x Time	Saline	20	Saline	50	72	-1.06	1.0
Cond x Time	Saline	20	Saline/cryo	0	72	0.43	1.0
Cond x Time	Saline	20	Saline/cryo	20	72	30.15	<.0001*
Cond x Time	Saline	20	Saline/cryo	50	72	11.12	<.0001*
Cond x Time	Saline	20	Saline/sham	0	72	0.11	1.0
Cond x Time	Saline	20	Saline/sham	20	72	0.05	1.0
Cond x Time	Saline	20	Saline/sham	50	72	-0.92	1.0
Cond x Time	Saline	20	No saline	0	72	0.95	1.0
Cond x Time	Saline	20	No saline	20	72	0.80	1.0
Cond x Time	Saline	20	No saline	50	72	0.90	.99
Cond x Time	Saline	50	Saline/cryo	0	72	1.21	.99
Cond x Time	Saline	50	Saline/cryo	20	72	30.93	<.0001*
Cond x Time	Saline	50	Saline/cryo	50	72	11.91	<.0001*
Cond x Time	Saline	50	Saline/sham	0	72	0.89	1.0
Cond x Time	Saline	50	Saline/sham	20	72	0.84	1.0
Cond x Time	Saline	50	Saline/sham	50	72	-0.14	1.0
Cond x Time	Saline	50	No saline	0	72	1.74	.84
Cond x Time	Saline	50	No saline	20	72	1.58	.91
Cond x Time	Saline	50	No saline	50	72	1.68	.87
Cond x Time	Saline/cryo	0	Saline/cryo	20	72	40.24	<.0001*
Cond x Time	Saline/cryo	0	Saline/cryo	50	72	14.49	<.0001*
Cond x Time	Saline/cryo	0	Saline/sham	0	72	-0.32	1.0
Cond x Time	Saline/cryo	0	Saline/sham	20	72	-0.37	1.0
Cond x Time	Saline/cryo	0	Saline/sham	50	72	-1.35	.97
Cond x Time	Saline/cryo	0	No saline	0	72	0.53	1.0
Cond x Time	Saline/cryo	0	No saline	20	72	0.37	1.0
Cond x Time	Saline/cryo	0	No saline	50	72	0.48	1.0
Cond x Time	Saline/cryo	20	Saline/cryo	50	72	-25.75	<.0001*
Cond x Time	Saline/cryo	20	Saline/sham	0	72	-30.04	<.0001*
Cond x Time	Saline/cryo	20	Saline/sham	20	72	-30.09	<.0001*
Cond x Time	Saline/cryo	20	Saline/sham	50	72	-31.07	<.0001*
Cond x Time	Saline/cryo	20	No saline	0	72	-29.19	<.0001*
Cond x Time	Saline/cryo	20	No saline	20	72	-29.35	<.0001*
Cond x Time	Saline/cryo	20	No saline	50	72	-29.24	<.0001*
Cond x Time	Saline/cryo	50	Saline/sham	0	72	-11.02	<.0001*
Cond x Time	Saline/cryo	50	Saline/sham	20	72	-11.07	<.0001*
Cond x Time	Saline/cryo	50	Saline/sham	50	72	-12.05	<.0001*
Cond x Time	Saline/cryo	50	No saline	0	72	-10.17	<.0001*
Cond x Time	Saline/cryo	50	No saline	20	72	-10.33	<.0001*

Table C 42. Continued

Cond x Time	Saline/cryo	50	No saline	50	72	-10.22	<.0001*
Cond x Time	Saline/sham	0	Saline/sham	20	72	-0.07	.94
Cond x Time	Saline/sham	0	Saline/sham	50	72	-1.39	.17
Cond x Time	Saline/sham	0	No saline	0	72	0.85	.40
Cond x Time	Saline/sham	0	No saline	20	72	0.69	.49
Cond x Time	Saline/sham	0	No saline	50	72	0.79	.43
Cond x Time	Saline/sham	20	Saline/sham	50	72	-1.32	.19
Cond x Time	Saline/sham	20	No saline	0	72	0.90	.37
Cond x Time	Saline/sham	20	No saline	20	72	0.75	.46
Cond x Time	Saline/sham	20	No saline	50	72	0.85	.40
Cond x Time	Saline/sham	50	No saline	0	72	1.88	.06
Cond x Time	Saline/sham	50	No saline	20	72	1.72	.09
Cond x Time	Saline/sham	50	No saline	50	72	1.82	.07
Cond x Time	No saline	0	No saline	20	72	-0.21	.83
Cond x Time	No saline	0	No saline	50	72	-0.07	.94
Cond x Time	No saline	20	No saline	50	72	0.14	.89

* = represents a significant difference
0 = pre
20 = $post_{tx}$
50 = 30 min $post_{tx}$

Table C 43. Ambient Surface Temperature (°C) for each Condition Across Time. Measures were Taken at the Last Minute During the 3 Application Phases (n = 3 Measures/Condition; Mean ± SD)

Condition	0	20	50
Saline	21.1 ± 0.5	21.0 ± 0.4	21.1 ± 0.3
Saline/cryo	21.1 ± 0.4	21.1 ± 0.5	21.1 ± 0.4
Saline/sham	21.1 ± 0.5	21.0 ± 0.4	21.0 ± 0.5
No saline	21.2 ± 0.5	21.0 ± 0.7	21.2 ± 0.6

Table C 44. Mixed Model Procedures for Fixed Effects Differences Between Condition and Time for Ambient Air Temperature

Effect	Numerator Degrees of Freedom	Denominator Degrees of Freedom	F-value	*P*-value
Time	2	72	1.4	0.24
Condition	3	72	0.1	0.97
Cond x Time	6	72	0.8	0.61

Table C 45. Least Square Means Differences Between Condition and Time for Ambient Air Temperature

Effect	Cond	Time	Cond	Time	Error	DF	t-value	*P*-value
Cond x Time	Saline	0	Saline	20	0.11	72	0.95	.35
Cond x Time	Saline	0	Saline	50	0.11	72	0.19	.85
Cond x Time	Saline	0	Saline/cryo	0	0.21	72	0.30	.77
Cond x Time	Saline	0	Saline/cryo	20	0.21	72	0.22	.83
Cond x Time	Saline	0	Saline/cryo	50	0.21	72	0.25	.81
Cond x Time	Saline	0	Saline/sham	0	0.21	72	0.35	.73
Cond x Time	Saline	0	Saline/sham	20	0.21	72	0.52	.60
Cond x Time	Saline	0	Saline/sham	50	0.21	72	0.81	.42
Cond x Time	Saline	0	No saline	0	0.21	72	-0.34	.74
Cond x Time	Saline	0	No saline	20	0.21	72	0.85	.40
Cond x Time	Saline	0	No saline	50	0.21	72	-0.04	.97
Cond x Time	Saline	20	Saline	50	0.11	72	-0.76	.45
Cond x Time	Saline	20	Saline/cryo	0	0.21	72	-0.20	.84
Cond x Time	Saline	20	Saline/cryo	20	0.21	72	-0.28	.78
Cond x Time	Saline	20	Saline/cryo	50	0.21	72	-0.25	.81
Cond x Time	Saline	20	Saline/sham	0	0.21	72	-0.15	.88
Cond x Time	Saline	20	Saline/sham	20	0.21	72	0.03	.98
Cond x Time	Saline	20	Saline/sham	50	0.21	72	0.31	.76
Cond x Time	Saline	20	No saline	0	0.21	72	-0.83	.41
Cond x Time	Saline	20	No saline	20	0.21	72	0.36	.72
Cond x Time	Saline	20	No saline	50	0.21	72	-0.54	.59
Cond x Time	Saline	50	Saline/cryo	0	0.21	72	0.20	.84
Cond x Time	Saline	50	Saline/cryo	20	0.21	72	0.12	.90
Cond x Time	Saline	50	Saline/cryo	50	0.21	72	0.15	.88
Cond x Time	Saline	50	Saline/sham	0	0.21	72	0.25	.81
Cond x Time	Saline	50	Saline/sham	20	0.21	72	0.43	.67
Cond x Time	Saline	50	Saline/sham	50	0.21	72	0.71	.48
Cond x Time	Saline	50	No saline	0	0.21	72	-0.43	.67
Cond x Time	Saline	50	No saline	20	0.21	72	0.75	.45
Cond x Time	Saline	50	No saline	50	0.21	72	-0.14	.89
Cond x Time	Saline/cryo	0	Saline/cryo	20	0.11	72	-0.15	.88
Cond x Time	Saline/cryo	0	Saline/cryo	50	0.11	72	-0.10	.92
Cond x Time	Saline/cryo	0	Saline/sham	0	0.21	72	0.05	.96
Cond x Time	Saline/cryo	0	Saline/sham	20	0.21	72	0.22	.82
Cond x Time	Saline/cryo	0	Saline/sham	50	0.21	72	0.51	.61
Cond x Time	Saline/cryo	0	No saline	0	0.21	72	-0.64	.53
Cond x Time	Saline/cryo	0	No saline	20	0.21	72	0.55	.58
Cond x Time	Saline/cryo	0	No saline	50	0.21	72	-0.34	.73
Cond x Time	Saline/cryo	20	Saline/cryo	55	0.11	72	0.05	.96
Cond x Time	Saline/cryo	20	Saline/sham	0	0.21	72	0.13	.90
Cond x Time	Saline/cryo	20	Saline/sham	20	0.21	72	0.30	.76
Cond x Time	Saline/cryo	20	Saline/sham	50	0.21	72	0.59	.56
Cond x Time	Saline/cryo	20	No saline	0	0.21	72	-0.56	.58
Cond x Time	Saline/cryo	20	No saline	20	0.21	72	0.63	.53
Cond x Time	Saline/cryo	20	No saline	50	0.21	72	-0.26	.79
Cond x Time	Saline/cryo	50	Saline/sham	0	0.21	72	0.10	.92
Cond x Time	Saline/cryo	50	Saline/sham	20	0.21	72	0.28	.78
Cond x Time	Saline/cryo	50	Saline/sham	50	0.21	72	0.56	.58
Cond x Time	Saline/cryo	50	No saline	0	0.21	72	-0.58	.56
Cond x Time	Saline/cryo	50	No saline	20	0.21	72	0.60	.55

Table C 45. Continued

Cond x Time	Saline/cryo	50	No saline	50	0.21	72	-0.29	.77
Cond x Time	Saline/sham	0	Saline/sham	20	0.11	72	0.34	.73
Cond x Time	Saline/sham	0	Saline/sham	50	0.11	72	0.89	.38
Cond x Time	Saline/sham	0	No saline	0	0.21	72	-0.68	.50
Cond x Time	Saline/sham	0	No saline	20	0.21	72	0.50	.62
Cond x Time	Saline/sham	0	No saline	50	0.21	72	-0.39	.70
Cond x Time	Saline/sham	20	Saline/sham	50	0.11	72	0.55	.59
Cond x Time	Saline/sham	20	No saline	0	0.21	72	-0.86	.39
Cond x Time	Saline/sham	20	No saline	20	0.21	72	0.33	.74
Cond x Time	Saline/sham	20	No saline	50	0.21	72	-0.57	.57
Cond x Time	Saline/sham	50	No saline	0	0.21	72	-1.14	.26
Cond x Time	Saline/sham	50	No saline	20	0.21	72	0.04	.97
Cond x Time	Saline/sham	50	No saline	50	0.21	72	-0.85	.40
Cond x Time	No saline	0	No saline	20	0.11	72	2.28	.03*
Cond x Time	No saline	0	No saline	50	0.11	72	0.56	.57
Cond x Time	No saline	20	No saline	50	0.11	72	-1.71	.09

* = represents a significant difference

0 = pre

20 = $post_{tx}$

50 = 30 min $post_{tx}$

Table C 46. All Data for each Subject Stacked

Sub	Cond	Time	Phase	PRI	VAS	H:M	Pop.	Pat.	Amb.
1	4	0	0	0	0	0.56	32.6	27.3	21.4
1	4	1	0				32.7	27.4	21.3
1	4	2	0				32.8	27.4	21.2
1	4	3	0				32.9	27.4	21.3
1	4	4	0				33.0	27.3	21.4
1	4	5	0				33.1	27.4	21.0
1	4	6	1				33.1	27.4	21.4
1	4	7	1				33.2	27.4	21.5
1	4	8	1				33.2	27.4	21.3
1	4	9	1				33.3	27.3	21.3
1	4	10	1				33.4	27.3	21.4
1	4	11	1				33.4	27.4	21.6
1	4	12	1				33.4	27.3	21.4
1	4	13	1				33.4	27.3	21.1
1	4	14	1				33.5	27.3	21.5
1	4	15	1				33.5	27.3	21.3
1	4	16	1				33.5	27.4	21.1
1	4	17	1				33.5	27.3	21.1
1	4	18	1				33.5	27.3	21.1
1	4	19	1				33.5	27.2	21.3
1	4	20	1				33.5	27.3	21.4
1	4	21	1				33.6	27.3	21.3
1	4	22	1				33.6	27.4	21.3
1	4	23	1				33.6	27.3	21.2
1	4	24	1				33.7	27.3	21.4
1	4	25	1	3	4	0.56	33.7	27.3	21.3
1	4	26	2				33.7	27.3	21.3
1	4	27	2				33.7	27.2	21.3
1	4	28	2				33.7	27.2	21.7
1	4	29	2				33.7	27.3	21.5
1	4	30	2				33.8	27.2	21.7
1	4	31	2				33.7	27.1	21.1
1	4	32	2				33.7	27.2	21.4
1	4	33	2				33.8	27.2	21.2
1	4	34	2				33.7	27.1	21.3
1	4	35	2				33.7	27.1	21.4
1	4	36	2				33.7	27.0	21.3
1	4	37	2				33.7	27.1	21.2
1	4	38	2				33.7	27.2	21.1
1	4	39	2				33.7	27.0	21.3
1	4	40	2				33.7	27.1	21.3
1	4	41	2				33.8	27.2	21.2
1	4	42	2				33.8	27.1	21.4
1	4	43	2				33.8	27.1	21.4
1	4	44	2				33.8	27.0	21.2
1	4	45	2				33.8	27.1	21.2

Table C 46. Continued

1	4	46	2				33.8	27.0	21.2
1	4	47	2				33.8	27.1	21.3
1	4	48	2				33.8	27.1	21.4
1	4	49	2				33.8	27.2	21.2
1	4	50	2				33.8	27.2	21.2
1	4	51	2				33.8	27.0	21.3
1	4	52	2				33.8	27.3	21.2
1	4	53	2				33.9	27.3	21.5
1	4	54	2				33.2	27.5	21.5
1	4	55	2	2	2	0.56	33.6	27.6	21.5
2	2	0	0	0	0	0.36	32.6	27.7	21.3
2	2	1	0				32.7	27.7	21.5
2	2	2	0				32.8	27.7	21.1
2	2	3	0				32.8	27.7	21.2
2	2	4	0				32.9	27.7	21.5
2	2	5	0				32.9	27.5	21.3
2	2	6	1				29.0	19.1	21.6
2	2	7	1				26.4	15.8	21.4
2	2	8	1				24.4	13.9	21.6
2	2	9	1				22.8	12.6	21.4
2	2	10	1				21.5	11.8	21.9
2	2	11	1				20.6	11.8	21.8
2	2	12	1				19.8	11.4	21.5
2	2	13	1				19.0	10.7	21.3
2	2	14	1				18.4	10.1	21.5
2	2	15	1				17.9	9.6	21.4
2	2	16	1				17.5	9.2	21.4
2	2	17	1				17.0	8.8	21.5
2	2	18	1				16.6	8.4	21.3
2	2	19	1				16.2	8.0	21.5
2	2	20	1				15.8	7.6	21.3
2	2	21	1				15.6	7.3	21.5
2	2	22	1				15.3	6.9	21.4
2	2	23	1				14.9	6.7	21.4
2	2	24	1				14.6	6.4	21.3
2	2	25	1	13	29	0.60	14.9	6.1	21.6
2	2	26	2				17.1	9.8	21.4
2	2	27	2				18.0	11.0	21.4
2	2	28	2				18.7	11.8	21.3
2	2	29	2				19.3	12.3	21.2
2	2	30	2				19.9	13.0	21.4
2	2	31	2				20.4	13.6	21.5
2	2	32	2				20.8	13.8	21.3
2	2	33	2				21.2	14.3	21.3
2	2	34	2				21.6	14.4	21.2
2	2	35	2				22.0	15.3	21.2
2	2	36	2				22.4	15.6	21.3

Table C 46. Continued

2	2	37	2				22.7	15.8	21.1
2	2	38	2				23.0	16.1	21.2
2	2	39	2				23.4	16.3	20.9
2	2	40	2				23.7	16.6	21.4
2	2	41	2				24.0	16.8	21.3
2	2	42	2				24.3	16.9	21.4
2	2	43	2				24.5	17.1	21.3
2	2	44	2				24.8	17.3	21.5
2	2	45	2				25.1	17.5	21.2
2	2	46	2				25.3	17.7	21.2
2	2	47	2				25.5	17.9	21.2
2	2	48	2				25.7	18.1	21.3
2	2	49	2				26.0	18.3	21.6
2	2	50	2				26.2	18.4	21.4
2	2	51	2				26.4	18.6	21.6
2	2	52	2				26.5	18.8	21.5
2	2	53	2				26.7	19.0	21.4
2	2	54	2				26.9	19.1	21.4
2	2	55	2	5	10	0.42	27.0	19.2	21.4
3	4	0	0	0	0	0.18	30.8	26.0	21.2
3	4	1	0				31.3	26.1	20.9
3	4	2	0				31.8	26.2	21.1
3	4	3	0				32.0	26.4	20.6
3	4	4	0				32.2	26.6	20.5
3	4	5	0				32.4	26.6	20.7
3	4	6	1				32.5	26.6	20.5
3	4	7	1				32.7	26.8	20.6
3	4	8	1				32.8	26.7	20.6
3	4	9	1				33.0	26.8	20.5
3	4	10	1				33.0	26.9	20.7
3	4	11	1				32.9	26.9	20.7
3	4	12	1				33.0	27.0	20.5
3	4	13	1				33.4	27.0	20.8
3	4	14	1				33.6	27.0	20.6
3	4	15	1				33.8	26.9	20.7
3	4	16	1				33.9	27.1	20.6
3	4	17	1				34.0	27.1	20.9
3	4	18	1				34.2	26.9	21.0
3	4	19	1				34.3	27.0	20.8
3	4	20	1				34.5	27.1	20.9
3	4	21	1				34.6	26.9	20.5
3	4	22	1				34.7	27.1	20.7
3	4	23	1				34.8	27.1	20.8
3	4	24	1				34.8	27.1	20.7
3	4	25	1	0	0	0.09	34.9	27.2	20.5
3	4	26	2				34.9	27.0	20.7
3	4	27	2				35.0	27.1	20.8

Table C 46. Continued

3	4	28	2				35.0	27.1	20.9
3	4	29	2				35.0	27.1	20.8
3	4	30	2				35.0	27.2	20.5
3	4	31	2				35.1	27.2	20.8
3	4	32	2				35.1	27.0	20.8
3	4	33	2				35.1	27.0	20.8
3	4	34	2				35.1	26.9	20.6
3	4	35	2				35.1	27.0	20.5
3	4	36	2				35.0	26.8	21.0
3	4	37	2				34.5	27.2	20.9
3	4	38	2				34.4	27.2	21.0
3	4	39	2				34.3	27.2	21.1
3	4	40	2				34.4	27.1	21.0
3	4	41	2				34.3	27.1	21.0
3	4	42	2				34.3	27.2	20.5
3	4	43	2				34.3	27.2	20.9
3	4	44	2				34.3	27.0	21.1
3	4	45	2				34.3	27.1	20.6
3	4	46	2				34.3	27.2	21.1
3	4	47	2				34.3	27.2	21.1
3	4	48	2				34.3	27.0	20.6
3	4	49	2				34.3	27.1	20.8
3	4	50	2				34.3	27.1	21.0
3	4	51	2				34.2	27.1	20.8
3	4	52	2				34.2	27.0	20.8
3	4	53	2				34.2	27.0	20.8
3	4	54	2				34.2	27.0	21.1
3	4	55	2	1	0	0.06	34.2	27.1	20.8
4	1	0	0	0	0	0.57	33.5	27.0	21.3
4	1	1	0				33.5	26.9	21.4
4	1	2	0				33.6	27.1	21.5
4	1	3	0				33.6	27.0	21.1
4	1	4	0				33.6	27.0	21.2
4	1	5	0				33.6	27.0	21.0
4	1	6	1				33.6	26.9	21.5
4	1	7	1				33.7	27.1	21.4
4	1	8	1				33.7	27.1	21.1
4	1	9	1				33.7	27.0	21.2
4	1	10	1				33.7	27.2	21.6
4	1	11	1				33.7	27.3	21.6
4	1	12	1				33.7	27.1	21.5
4	1	13	1				33.7	27.1	21.4
4	1	14	1				33.8	27.0	21.4
4	1	15	1				33.8	27.0	21.4
4	1	16	1				33.8	27.1	21.5
4	1	17	1				33.8	27.1	21.1
4	1	18	1				33.8	27.2	21.4

Table C 46. Continued

4	1	19	1				33.8	27.0	21.4
4	1	20	1				33.8	27.1	21.5
4	1	21	1				33.8	26.8	21.1
4	1	22	1				33.7	26.9	21.2
4	1	23	1				33.8	26.8	21.2
4	1	24	1				33.8	26.9	21.3
4	1	25	1	40	77	0.59	33.8	27.0	21.4
4	1	26	2				33.8	27.1	21.2
4	1	27	2				33.8	27.0	21.0
4	1	28	2				33.8	27.1	21.3
4	1	29	2				33.8	26.7	21.5
4	1	30	2				33.7	26.8	21.2
4	1	31	2				33.8	26.9	21.4
4	1	32	2				33.7	26.9	21.5
4	1	33	2				33.7	27.1	21.2
4	1	34	2				33.7	27.1	21.4
4	1	35	2				33.7	27.3	21.6
4	1	36	2				33.8	27.3	21.4
4	1	37	2				33.8	27.4	21.4
4	1	38	2				33.8	27.5	21.4
4	1	39	2				33.8	27.4	21.3
4	1	40	2				33.8	27.5	21.2
4	1	41	2				33.8	27.5	21.4
4	1	42	2				33.8	27.4	21.2
4	1	43	2				33.8	27.5	21.4
4	1	44	2				33.8	27.6	21.3
4	1	45	2				33.9	27.5	21.2
4	1	46	2				33.9	27.6	21.5
4	1	47	2				33.9	27.5	21.3
4	1	48	2				33.9	27.6	21.4
4	1	49	2				33.8	27.7	21.3
4	1	50	2				33.9	27.7	21.2
4	1	51	2				33.9	27.7	21.4
4	1	52	2				33.9	27.0	21.4
4	1	53	2				33.9	27.2	21.5
4	1	54	2				33.8	27.3	21.4
4	1	55	2	20	14	0.53	33.8	27.2	21.6
5	1	0	0	0	0	0.29	33.9	28.8	21.5
5	1	1	0				33.9	28.5	21.6
5	1	2	0				34.1	28.6	21.0
5	1	3	0				34.0	28.6	21.6
5	1	4	0				33.9	28.5	21.5
5	1	5	0				33.9	28.2	21.0
5	1	6	1				33.8	28.1	21.3
5	1	7	1				34.0	28.3	21.4
5	1	8	1				34.1	28.2	21.4
5	1	9	1				34.1	28.1	21.3

Table C 46. Continued

5	1	10	1				34.0	28.2	21.3
5	1	11	1				34.0	28.1	21.4
5	1	12	1				33.9	28.1	21.6
5	1	13	1				33.9	28.1	21.5
5	1	14	1				34.0	28.0	21.4
5	1	15	1				34.1	27.9	21.4
5	1	16	1				34.1	28.1	21.6
5	1	17	1				34.2	28.1	21.4
5	1	18	1				34.3	28.1	21.5
5	1	19	1				34.3	28.1	21.5
5	1	20	1				34.3	28.2	21.4
5	1	21	1				34.3	28.2	21.4
5	1	22	1				34.4	28.3	21.6
5	1	23	1				34.3	28.3	21.6
5	1	24	1				34.3	28.3	21.4
5	1	25	1	23	70	0.18	34.3	28.4	21.5
5	1	26	2				34.3	28.2	21.1
5	1	27	2				34.2	28.1	21.4
5	1	28	2				34.2	28.2	21.4
5	1	29	2				34.3	28.2	21.6
5	1	30	2				34.3	28.2	21.5
5	1	31	2				34.3	28.1	21.6
5	1	32	2				34.3	28.2	21.2
5	1	33	2				34.3	28.1	21.4
5	1	34	2				34.3	28.0	21.4
5	1	35	2				34.3	28.1	21.5
5	1	36	2				34.3	27.9	21.2
5	1	37	2				34.3	27.9	21.6
5	1	38	2				34.3	27.9	21.5
5	1	39	2				34.4	27.9	21.5
5	1	40	2				34.4	27.9	21.4
5	1	41	2				34.4	28.0	21.4
5	1	42	2				34.5	27.9	21.1
5	1	43	2				34.5	27.9	21.3
5	1	44	2				34.6	27.9	21.4
5	1	45	2				34.6	27.9	21.5
5	1	46	2				34.6	28.1	21.4
5	1	47	2				34.6	28.2	21.5
5	1	48	2				34.6	28.1	21.3
5	1	49	2				34.6	28.0	21.4
5	1	50	2				34.7	28.2	21.3
5	1	51	2				34.7	28.0	21.5
5	1	52	2				34.7	28.0	21.1
5	1	53	2				34.6	28.1	21.2
5	1	54	2				34.6	28.1	21.4
5	1	55	2	1	0	0.22	34.6	28.1	21.2
6	2	0	0	0	0	0.31	33.2	26.8	20.9

Table C 46. Continued

6	2	1	0				33.3	26.8	20.8
6	2	2	0				33.5	26.8	21.0
6	2	3	0				33.5	26.8	20.9
6	2	4	0				33.5	26.9	20.8
6	2	5	0				33.3	23.9	20.8
6	2	6	1				11.4	18.7	20.8
6	2	7	1				9.7	15.1	21.1
6	2	8	1				7.9	13.4	21.1
6	2	9	1				7.4	12.6	21.0
6	2	10	1				7.3	11.3	20.8
6	2	11	1				8.0	10.4	21.0
6	2	12	1				8.3	9.6	20.7
6	2	13	1				8.1	9.4	20.9
6	2	14	1				7.7	8.8	20.9
6	2	15	1				7.2	8.3	20.8
6	2	16	1				6.7	7.9	20.9
6	2	17	1				6.5	7.6	20.8
6	2	18	1				6.3	7.3	20.9
6	2	19	1				6.3	6.9	21.1
6	2	20	1				6.1	6.7	21.0
6	2	21	1				5.8	6.6	21.1
6	2	22	1				5.1	6.5	20.8
6	2	23	1				5.3	6.5	21.0
6	2	24	1				5.2	6.3	21.0
6	2	25	1	19	31	0.67	5.2	6.1	21.0
6	2	26	2				5.5	6.1	20.9
6	2	27	2				7.7	7.0	20.9
6	2	28	2				14.1	9.4	21.2
6	2	29	2				17.1	10.6	21.0
6	2	30	2				19.2	11.4	20.9
6	2	31	2				20.6	12.0	21.1
6	2	32	2				21.7	12.6	20.9
6	2	33	2				22.5	13.0	20.8
6	2	34	2				23.6	13.6	21.1
6	2	35	2				24.2	14.0	20.8
6	2	36	2				24.9	14.6	20.7
6	2	37	2				25.6	15.0	20.7
6	2	38	2				26.1	15.5	20.8
6	2	39	2				26.7	15.9	20.9
6	2	40	2				27.2	16.2	20.9
6	2	41	2				27.7	16.6	21.2
6	2	42	2				28.2	17.0	20.9
6	2	43	2				28.7	17.3	21.0
6	2	44	2				29.0	17.6	21.0
6	2	45	2				29.3	17.8	20.9
6	2	46	2				29.6	18.1	21.0
6	2	47	2				29.9	18.3	20.5

Table C 46. Continued

6	2	48	2				30.2	18.5	20.9
6	2	49	2				30.4	18.8	20.9
6	2	50	2				30.6	19.0	20.9
6	2	51	2				30.7	19.2	21.2
6	2	52	2				30.9	19.4	21.1
6	2	53	2				31.0	19.6	20.9
6	2	54	2				31.2	19.8	21.0
6	2	55	2	14	20	0.23	31.3	19.9	20.8
7	2	0	0	0	0	0.28	32.8	27.4	20.4
7	2	1	0				32.8	27.6	20.4
7	2	2	0				32.9	27.4	20.3
7	2	3	0				32.9	27.3	20.0
7	2	4	0				32.9	27.4	20.4
7	2	5	0				32.4	21.9	20.6
7	2	6	1				21.4	17.6	20.7
7	2	7	1				18.7	16.1	20.6
7	2	8	1				15.2	13.9	20.9
7	2	9	1				12.6	12.0	20.8
7	2	10	1				10.8	10.7	20.4
7	2	11	1				9.6	9.8	20.6
7	2	12	1				8.8	8.9	20.3
7	2	13	1				8.1	8.4	20.0
7	2	14	1				7.6	8.0	20.5
7	2	15	1				7.1	7.6	20.7
7	2	16	1				6.5	7.4	20.3
7	2	17	1				6.4	7.0	20.7
7	2	18	1				6.5	6.6	20.4
7	2	19	1				6.2	6.3	20.4
7	2	20	1				6.0	5.9	20.6
7	2	21	1				5.8	5.8	20.4
7	2	22	1				5.9	5.6	20.5
7	2	23	1				5.7	5.4	20.7
7	2	24	1				5.6	5.2	20.3
7	2	25	1	7	29	0.42	5.5	5.0	20.5
7	2	26	2				8.1	5.7	20.4
7	2	27	2				10.7	7.0	20.6
7	2	28	2				11.8	7.7	20.3
7	2	29	2				12.9	8.5	20.3
7	2	30	2				13.8	8.8	20.5
7	2	31	2				14.7	9.2	20.2
7	2	32	2				15.5	9.8	20.2
7	2	33	2				16.2	10.2	20.3
7	2	34	2				16.8	10.6	20.4
7	2	35	2				17.4	10.8	20.8
7	2	36	2				18.1	11.2	20.5
7	2	37	2				18.8	11.5	20.5
7	2	38	2				19.4	11.8	20.3

Table C 46. Continued

7	2	39	2				20.0	12.1	20.0
7	2	40	2				20.5	12.4	20.0
7	2	41	2				20.9	12.7	20.5
7	2	42	2				21.4	13.1	21.1
7	2	43	2				21.8	13.3	20.3
7	2	44	2				22.1	13.7	20.7
7	2	45	2				22.4	14.0	20.6
7	2	46	2				22.8	14.2	20.3
7	2	47	2				23.1	14.4	20.6
7	2	48	2				23.4	14.7	20.2
7	2	49	2				23.7	14.9	20.4
7	2	50	2				24.0	15.2	20.1
7	2	51	2				24.3	15.4	19.9
7	2	52	2				24.5	15.6	20.2
7	2	53	2				24.7	15.8	19.9
7	2	54	2				25.0	15.9	20.4
7	2	55	2	0	0	0.21	25.2	16.1	20.3
8	4	0	0	0	0	0.31	31.7	27.2	20.4
8	4	1	0				33.2	27.3	20.4
8	4	2	0				33.3	27.2	20.3
8	4	3	0				33.3	27.3	20.5
8	4	4	0				33.3	27.2	20.3
8	4	5	0				33.4	27.2	20.3
8	4	6	1				33.4	27.2	20.8
8	4	7	1				33.4	27.2	20.2
8	4	8	1				33.4	27.2	20.6
8	4	9	1				33.4	27.2	19.9
8	4	10	1				33.4	27.1	20.4
8	4	11	1				33.5	27.2	20.0
8	4	12	1				33.5	27.2	20.1
8	4	13	1				33.5	27.2	20.6
8	4	14	1				33.5	27.2	19.7
8	4	15	1				33.5	27.2	20.1
8	4	16	1				33.5	27.1	20.4
8	4	17	1				33.5	27.1	20.3
8	4	18	1				33.5	27.1	20.6
8	4	19	1				33.5	27.1	20.3
8	4	20	1				33.5	27.1	20.7
8	4	21	1				33.5	27.1	20.1
8	4	22	1				33.5	27.1	20.4
8	4	23	1				33.5	27.1	20.3
8	4	24	1				33.5	27.1	20.5
8	4	25	1	2	1	0.39	33.5	27.0	19.9
8	4	26	2				33.5	27.1	20.3
8	4	27	2				33.5	27.0	20.6
8	4	28	2				33.5	27.0	20.6
8	4	29	2				33.5	27.0	20.4

Table C 46. Continued

8	4	30	2				33.5	26.9	20.6
8	4	31	2				33.5	27.0	20.3
8	4	32	2				33.5	26.9	20.0
8	4	33	2				33.5	26.8	20.3
8	4	34	2				33.5	26.8	20.2
8	4	35	2				33.5	26.9	20.4
8	4	36	2				33.5	26.9	20.3
8	4	37	2				33.5	26.8	20.7
8	4	38	2				33.5	26.8	20.2
8	4	39	2				33.5	26.8	20.6
8	4	40	2				33.5	26.8	20.6
8	4	41	2				33.5	26.7	20.5
8	4	42	2				33.5	27.2	20.3
8	4	43	2				33.5	26.9	20.5
8	4	44	2				33.5	26.9	20.3
8	4	45	2				33.5	26.8	20.6
8	4	46	2				33.4	26.7	20.5
8	4	47	2				33.4	26.8	20.1
8	4	48	2				33.4	26.8	20.3
8	4	49	2				33.4	26.8	20.3
8	4	50	2				33.5	26.8	20.5
8	4	51	2				33.4	26.8	20.1
8	4	52	2				33.5	26.8	20.3
8	4	53	2				33.4	26.7	20.0
8	4	54	2				33.4	26.8	19.7
8	4	55	2	0	0	0.39	33.4	26.8	20.4
9	4	0	0	0	0	0.45	32.7	28.2	21.1
9	4	1	0				32.7	28.0	20.9
9	4	2	0				32.8	28.3	21.2
9	4	3	0				33.0	28.2	21.0
9	4	4	0				33.1	28.1	20.9
9	4	5	0				33.2	28.1	20.7
9	4	6	1				33.3	28.1	20.5
9	4	7	1				33.3	28.1	20.3
9	4	8	1				33.4	28.1	20.8
9	4	9	1				33.5	28.1	20.6
9	4	10	1				33.5	28.1	20.7
9	4	11	1				33.6	28.0	20.5
9	4	12	1				33.6	28.1	21.0
9	4	13	1				33.7	28.1	21.0
9	4	14	1				33.7	28.1	20.5
9	4	15	1				33.8	28.1	20.8
9	4	16	1				33.8	28.1	21.1
9	4	17	1				33.8	28.2	20.9
9	4	18	1				33.8	28.1	20.5
9	4	19	1				33.8	28.1	20.3
9	4	20	1				33.8	28.3	20.4

Table C 46. Continued

9	4	21	1				33.9	28.3	20.8
9	4	22	1				33.9	28.3	20.5
9	4	23	1				33.9	28.3	21.1
9	4	24	1				34.0	28.2	20.7
9	4	25	1	1	0	0.42	33.8	28.2	20.9
9	4	26	2				33.7	28.1	20.5
9	4	27	2				33.7	28.0	20.3
9	4	28	2				33.7	28.0	20.4
9	4	29	2				33.6	28.0	20.3
9	4	30	2				33.9	27.9	20.7
9	4	31	2				34.0	27.9	20.8
9	4	32	2				34.0	27.9	20.4
9	4	33	2				34.0	28.0	20.5
9	4	34	2				34.0	27.9	20.5
9	4	35	2				34.0	28.0	20.2
9	4	36	2				34.1	27.9	20.6
9	4	37	2				34.1	28.0	20.4
9	4	38	2				34.2	27.9	20.6
9	4	39	2				34.2	28.0	20.9
9	4	40	2				34.3	28.1	20.3
9	4	41	2				34.3	28.0	20.8
9	4	42	2				34.3	28.0	20.7
9	4	43	2				34.3	28.1	20.8
9	4	44	2				34.3	28.0	20.4
9	4	45	2				34.4	28.1	20.7
9	4	46	2				34.4	28.0	20.4
9	4	47	2				34.4	28.1	20.4
9	4	48	2				34.5	28.1	20.0
9	4	49	2				34.5	28.0	21.0
9	4	50	2				34.4	28.1	21.2
9	4	51	2				34.3	28.0	20.7
9	4	52	2				34.3	28.0	20.7
9	4	53	2				34.2	27.9	20.3
9	4	54	2				34.2	28.0	20.5
9	4	55	2	0	0	0.41	34.2	28.0	20.6
10	1	0	0	0	0	0.70	33.9	28.8	21.5
10	1	1	0				33.9	28.5	21.6
10	1	2	0				34.1	28.6	21.0
10	1	3	0				34.0	28.6	21.6
10	1	4	0				33.9	28.5	21.5
10	1	5	0				33.9	28.2	21.0
10	1	6	1				33.8	28.1	21.3
10	1	7	1				34.0	28.3	21.4
10	1	8	1				34.1	28.2	21.4
10	1	9	1				34.1	28.1	21.3
10	1	10	1				34.0	28.2	21.3
10	1	11	1				34.0	28.1	21.4

Table C 46. Continued

10	1	12	1				33.9	28.1	21.6
10	1	13	1				33.9	28.1	21.5
10	1	14	1				34.0	28.0	21.4
10	1	15	1				34.1	27.9	21.4
10	1	16	1				34.1	28.1	21.6
10	1	17	1				34.2	28.1	21.4
10	1	18	1				34.3	28.1	21.5
10	1	19	1				34.3	28.1	21.5
10	1	20	1				34.3	28.2	21.4
10	1	21	1				34.3	28.2	21.4
10	1	22	1				34.4	28.3	21.6
10	1	23	1				34.3	28.3	21.6
10	1	24	1				34.3	28.3	21.4
10	1	25	1	7	21	0.54	34.3	28.4	21.5
10	1	26	2				34.3	28.2	21.1
10	1	27	2				34.2	28.1	21.4
10	1	28	2				34.2	28.2	21.4
10	1	29	2				34.3	28.2	21.6
10	1	30	2				34.3	28.2	21.5
10	1	31	2				34.3	28.1	21.6
10	1	32	2				34.3	28.2	21.2
10	1	33	2				34.3	28.1	21.4
10	1	34	2				34.3	28.0	21.4
10	1	35	2				34.3	28.1	21.5
10	1	36	2				34.3	27.9	21.2
10	1	37	2				34.3	27.9	21.6
10	1	38	2				34.3	27.9	21.5
10	1	39	2				34.4	27.9	21.5
10	1	40	2				34.4	27.9	21.4
10	1	41	2				34.4	28.0	21.4
10	1	42	2				34.5	27.9	21.1
10	1	43	2				34.5	27.9	21.3
10	1	44	2				34.6	27.9	21.4
10	1	45	2				34.6	27.9	21.5
10	1	46	2				34.6	28.1	21.4
10	1	47	2				34.6	28.2	21.5
10	1	48	2				34.6	28.1	21.3
10	1	49	2				34.6	28.0	21.4
10	1	50	2				34.7	28.2	21.3
10	1	51	2				34.7	28.0	21.5
10	1	52	2				34.7	28.0	21.1
10	1	53	2				34.6	28.1	21.2
10	1	54	2				34.6	28.1	21.4
10	1	55	2	7	6	0.62	34.6	28.1	21.4
11	3	0	0	0	0	0.60	31.5	28.3	20.5
11	3	1	0				31.5	27.6	21.2
11	3	2	0				31.3	27.9	21.4

Table C 46. Continued

11	3	3	0				31.3	27.9	21.3
11	3	4	0				31.4	27.9	21.1
11	3	5	0				31.5	27.9	21.3
11	3	6	1				31.6	28.0	20.7
11	3	7	1				31.7	28.0	20.6
11	3	8	1				31.8	28.2	20.8
11	3	9	1				31.9	28.3	20.7
11	3	10	1				32.0	28.4	20.6
11	3	11	1				32.2	28.4	21.1
11	3	12	1				32.2	28.5	21.1
11	3	13	1				32.4	28.5	20.9
11	3	14	1				32.4	28.6	20.7
11	3	15	1				32.5	28.7	21.2
11	3	16	1				32.6	28.7	21.2
11	3	17	1				32.7	28.8	20.9
11	3	18	1				32.8	28.9	20.8
11	3	19	1				32.9	29.0	20.7
11	3	20	1				33.0	29.1	20.6
11	3	21	1				33.0	29.2	20.8
11	3	22	1				31.0	28.9	20.9
11	3	23	1				29.9	29.0	21.4
11	3	24	1				29.4	29.1	21.2
11	3	25	1	21	58	0.22	29.8	29.0	20.7
11	3	26	2				30.2	29.1	21.3
11	3	27	2				30.6	29.1	20.9
11	3	28	2				31.0	29.1	20.8
11	3	29	2				31.3	29.1	20.6
11	3	30	2				31.6	29.2	21.0
11	3	31	2				31.9	29.4	20.6
11	3	32	2				32.1	29.4	20.7
11	3	33	2				32.3	29.5	20.8
11	3	34	2				32.4	29.6	20.7
11	3	35	2				32.6	29.6	21.0
11	3	36	2				32.6	29.7	20.8
11	3	37	2				32.7	29.6	20.9
11	3	38	2				32.8	29.7	20.7
11	3	39	2				32.9	29.6	20.5
11	3	40	2				32.9	29.7	20.3
11	3	41	2				33.0	29.7	20.5
11	3	42	2				33.0	29.7	20.8
11	3	43	2				33.0	29.6	20.9
11	3	44	2				33.0	29.8	20.5
11	3	45	2				33.1	29.7	20.7
11	3	46	2				33.1	29.7	20.6
11	3	47	2				33.1	29.7	20.9
11	3	48	2				33.1	29.8	20.9
11	3	49	2				33.1	29.8	21.0

Table C 46. Continued

11	3	50	2				33.1	29.7	20.9
11	3	51	2				33.1	29.8	20.9
11	3	52	2				33.0	29.8	20.9
11	3	53	2				33.0	29.7	20.8
11	3	54	2				33.0	29.7	20.8
11	3	55	2	0	5	0.21	32.9	29.7	21.5
12	2	0	0	0	0	0.58	33.0	28.4	20.8
12	2	1	0				33.0	28.4	21.3
12	2	2	0				33.0	28.3	21.0
12	2	3	0				33.0	28.4	21.1
12	2	4	0				29.6	19.3	21.6
12	2	5	0				10.5	20.9	21.2
12	2	6	1				5.6	13.4	21.2
12	2	7	1				4.8	15.5	21.2
12	2	8	1				5.4	11.0	21.2
12	2	9	1				3.8	7.7	21.0
12	2	10	1				3.9	10.5	21.4
12	2	11	1				4.0	10.5	21.1
12	2	12	1				4.4	6.3	21.4
12	2	13	1				4.2	7.4	21.0
12	2	14	1				3.8	9.9	21.2
12	2	15	1				3.4	9.7	20.9
12	2	16	1				3.4	9.7	21.1
12	2	17	1				3.2	9.8	21.1
12	2	18	1				2.9	9.5	21.2
12	2	19	1				3.0	9.4	21.4
12	2	20	1				3.4	8.9	21.0
12	2	21	1				3.3	8.4	21.1
12	2	22	1				3.7	7.9	21.3
12	2	23	1				5.0	8.6	21.3
12	2	24	1				5.0	8.5	21.3
12	2	25	1	20	32	0.63	5.9	8.4	21.3
12	2	26	2				10.5	10.9	21.0
12	2	27	2				12.2	11.7	21.2
12	2	28	2				13.8	12.5	21.5
12	2	29	2				15.4	13.1	21.2
12	2	30	2				16.7	13.8	21.0
12	2	31	2				17.9	14.4	21.0
12	2	32	2				19.0	14.8	21.1
12	2	33	2				19.9	15.2	21.5
12	2	34	2				20.6	15.6	21.2
12	2	35	2				21.3	15.9	21.2
12	2	36	2				22.0	16.3	21.1
12	2	37	2				22.5	16.6	21.0
12	2	38	2				23.0	17.0	20.8
12	2	39	2				23.5	17.3	20.9
12	2	40	2				24.0	17.6	20.9

Table C 46. Continued

12	2	41	2				24.5	17.9	20.8
12	2	42	2				24.9	18.1	21.1
12	2	43	2				25.4	18.4	21.2
12	2	44	2				25.7	18.6	20.8
12	2	45	2				26.1	18.9	21.1
12	2	46	2				26.4	19.1	21.0
12	2	47	2				26.7	19.3	21.1
12	2	48	2				27.0	19.5	21.0
12	2	49	2				27.3	19.7	21.1
12	2	50	2				27.5	19.9	20.9
12	2	51	2				27.7	20.0	21.0
12	2	52	2				28.0	20.2	21.1
12	2	53	2				28.2	20.3	21.2
12	2	54	2				28.3	20.5	21.0
12	2	55	2	17	25	0.64	28.5	20.6	21.2
13	3	0	0	0	0	0.34	31.1	27.1	21.8
13	3	1	0				31.3	27.2	21.6
13	3	2	0				31.4	27.3	21.8
13	3	3	0				31.6	27.3	21.6
13	3	4	0				31.8	27.4	21.2
13	3	5	0				31.9	27.4	21.4
13	3	6	1				32.0	27.5	21.4
13	3	7	1				32.1	27.4	21.5
13	3	8	1				32.1	27.6	21.3
13	3	9	1				32.3	27.7	21.3
13	3	10	1				32.4	27.7	21.4
13	3	11	1				32.5	27.7	21.6
13	3	12	1				32.5	27.7	21.3
13	3	13	1				32.5	27.8	21.4
13	3	14	1				32.6	27.6	21.4
13	3	15	1				31.8	27.5	21.4
13	3	16	1				31.3	27.2	21.4
13	3	17	1				30.7	27.2	21.5
13	3	18	1				30.6	27.2	21.6
13	3	19	1				30.7	27.1	21.5
13	3	20	1				30.9	27.2	21.5
13	3	21	1				31.1	27.2	21.5
13	3	22	1				31.2	27.2	21.5
13	3	23	1				31.2	27.2	21.5
13	3	24	1				31.4	27.2	21.4
13	3	25	1	10	15	0.10	31.5	27.3	21.4
13	3	26	2				31.5	27.3	21.2
13	3	27	2				31.6	27.4	21.5
13	3	28	2				31.7	27.4	21.6
13	3	29	2				31.4	26.9	21.4
13	3	30	2				31.8	27.4	21.7
13	3	31	2				32.0	27.7	21.6

Table C 46. Continued

13	3	32	2				31.9	27.7	21.6
13	3	33	2				31.1	27.5	21.5
13	3	34	2				31.2	27.6	21.3
13	3	35	2				31.1	27.7	21.5
13	3	36	2				31.1	27.7	21.6
13	3	37	2				31.1	27.7	21.7
13	3	38	2				31.1	27.7	21.5
13	3	39	2				31.0	27.8	21.4
13	3	40	2				31.2	28.0	21.4
13	3	41	2				31.3	28.2	21.6
13	3	42	2				31.5	28.4	21.4
13	3	43	2				31.6	28.4	21.4
13	3	44	2				31.8	28.5	21.4
13	3	45	2				32.0	28.6	21.3
13	3	46	2				32.2	28.6	21.5
13	3	47	2				32.3	28.6	21.5
13	3	48	2				32.4	28.6	21.3
13	3	49	2				32.5	28.6	21.5
13	3	50	2				32.6	28.5	21.5
13	3	51	2				32.6	28.4	21.4
13	3	52	2				32.6	28.4	21.6
13	3	53	2				32.6	28.4	21.4
13	3	54	2				32.7	28.4	21.5
13	3	55	2	2	3	0.10	32.7	28.3	21.3
14	4	0	0	0	0	0.41	31.6	27.6	20.8
14	4	1	0				31.6	27.6	20.7
14	4	2	0				31.8	27.7	20.6
14	4	3	0				31.9	27.6	21.1
14	4	4	0				32.1	27.7	20.6
14	4	5	0				32.3	27.8	20.7
14	4	6	1				32.3	27.9	20.7
14	4	7	1				32.5	27.8	20.8
14	4	8	1				32.6	27.8	20.6
14	4	9	1				32.8	27.8	20.7
14	4	10	1				32.9	27.8	20.8
14	4	11	1				33.0	27.7	20.6
14	4	12	1				33.1	27.7	20.7
14	4	13	1				33.2	27.7	20.9
14	4	14	1				33.2	27.7	20.8
14	4	15	1				33.2	27.7	20.7
14	4	16	1				33.2	27.7	20.7
14	4	17	1				33.2	27.7	20.6
14	4	18	1				33.2	27.7	20.8
14	4	19	1				33.2	27.8	20.5
14	4	20	1				33.2	27.7	20.7
14	4	21	1				33.2	27.6	20.8
14	4	22	1				33.2	27.7	21.0

Table C 46. Continued

14	4	23	1				33.1	27.7	20.5
14	4	24	1				33.1	27.7	20.8
14	4	25	1	1	2	0.41	33.1	27.7	20.5
14	4	26	2				33.0	27.8	20.8
14	4	27	2				33.0	27.6	20.7
14	4	28	2				32.9	27.7	20.6
14	4	29	2				32.9	27.7	20.7
14	4	30	2				32.8	27.6	20.8
14	4	31	2				32.7	27.6	20.6
14	4	32	2				32.8	27.4	20.6
14	4	33	2				32.8	27.5	20.5
14	4	34	2				32.9	27.6	20.7
14	4	35	2				33.0	27.6	20.7
14	4	36	2				33.0	27.5	20.2
14	4	37	2				33.1	27.5	20.6
14	4	38	2				33.2	27.4	20.7
14	4	39	2				33.2	27.5	20.7
14	4	40	2				33.2	27.4	20.7
14	4	41	2				33.2	27.5	20.9
14	4	42	2				33.3	27.5	20.1
14	4	43	2				33.2	27.5	20.7
14	4	44	2				33.3	27.5	20.7
14	4	45	2				33.3	27.6	20.8
14	4	46	2				33.3	27.5	21.0
14	4	47	2				33.3	27.5	20.5
14	4	48	2				33.3	27.4	20.7
14	4	49	2				33.3	27.5	20.8
14	4	50	2				33.3	27.5	20.3
14	4	51	2				33.3	27.5	20.7
14	4	52	2				33.2	27.5	20.7
14	4	53	2				33.2	27.5	20.9
14	4	54	2				33.2	27.7	20.5
14	4	55	2	1	2	0.43	33.2	27.6	20.8
15	3	0	0	0	0	0.48	32.1	26.7	21.3
15	3	1	0				32.3	26.8	21.2
15	3	2	0				32.5	26.9	20.6
15	3	3	0				32.6	26.9	20.6
15	3	4	0				32.6	26.9	20.8
15	3	5	0				32.7	26.9	20.4
15	3	6	1				32.8	27.0	20.7
15	3	7	1				32.9	27.0	20.7
15	3	8	1				33.0	27.1	20.8
15	3	9	1				33.1	27.1	20.6
15	3	10	1				33.1	27.1	20.9
15	3	11	1				33.2	27.1	20.4
15	3	12	1				33.1	27.1	20.5
15	3	13	1				32.0	27.2	20.3

Table C 46. Continued

15	3	14	1				32.2	26.8	20.7
15	3	15	1				32.2	26.7	20.6
15	3	16	1				32.3	26.7	20.3
15	3	17	1				32.4	26.7	20.5
15	3	18	1				32.4	26.7	20.7
15	3	19	1				32.5	26.7	20.5
15	3	20	1				32.7	26.7	20.9
15	3	21	1				32.8	26.7	20.9
15	3	22	1				32.9	26.8	21.0
15	3	23	1				32.9	26.7	20.6
15	3	24	1				33.0	26.7	20.6
15	3	25	1	16	69	0.42	33.1	26.8	20.5
15	3	26	2				33.2	26.8	20.9
15	3	27	2				33.2	26.8	20.7
15	3	28	2				33.1	26.8	20.6
15	3	29	2				33.2	26.8	20.2
15	3	30	2				33.2	26.8	20.8
15	3	31	2				33.2	26.8	20.4
15	3	32	2				33.1	26.9	20.8
15	3	33	2				31.8	26.7	20.4
15	3	34	2				30.4	26.5	20.7
15	3	35	2				31.2	26.3	21.2
15	3	36	2				31.6	26.2	21.5
15	3	37	2				31.9	26.2	20.8
15	3	38	2				32.1	26.2	20.7
15	3	39	2				32.3	26.2	20.7
15	3	40	2				30.8	26.2	20.8
15	3	41	2				30.9	26.3	20.4
15	3	42	2				31.1	26.4	20.6
15	3	43	2				31.5	26.4	20.5
15	3	44	2				31.8	26.4	20.8
15	3	45	2				32.0	26.5	20.5
15	3	46	2				32.1	26.5	20.7
15	3	47	2				32.2	26.5	20.8
15	3	48	2				32.3	26.5	20.3
15	3	49	2				32.5	26.5	20.6
15	3	50	2				32.5	26.5	20.6
15	3	51	2				32.6	26.5	20.8
15	3	52	2				32.7	26.5	20.9
15	3	53	2				32.7	26.5	20.6
15	3	54	2				32.8	26.5	20.7
15	3	55	2	3	16	0.39	32.8	26.5	20.7
16	2	0	0	0	0	0.24	32.9	27.8	20.9
16	2	1	0				32.9	27.7	20.8
16	2	2	0				32.9	27.7	20.6
16	2	3	0				32.8	27.7	21.2
16	2	4	0				32.9	27.7	21.3

Table C 46. Continued

16	2	5	0				32.9	27.5	21.2
16	2	6	1				21.8	20.6	21.2
16	2	7	1				8.8	16.6	21.5
16	2	8	1				9.6	14.7	21.0
16	2	9	1				8.8	12.2	21.1
16	2	10	1				7.8	9.0	21.1
16	2	11	1				6.9	9.3	20.8
16	2	12	1				6.8	7.4	21.0
16	2	13	1				7.1	7.5	21.1
16	2	14	1				6.5	6.3	21.2
16	2	15	1				6.2	7.2	21.1
16	2	16	1				6.0	6.2	21.1
16	2	17	1				6.3	5.8	20.9
16	2	18	1				6.1	5.4	21.3
16	2	19	1				6.1	4.8	21.1
16	2	20	1				6.0	5.1	21.1
16	2	21	1				5.7	5.0	21.0
16	2	22	1				5.3	4.6	21.2
16	2	23	1				5.5	4.5	21.2
16	2	24	1				5.6	4.5	21.1
16	2	25	1	11	28	0.39	5.5	4.4	20.9
16	2	26	2				10.1	11.0	21.1
16	2	27	2				13.2	10.7	21.4
16	2	28	2				15.6	11.4	21.5
16	2	29	2				17.6	12.0	21.3
16	2	30	2				19.2	12.8	21.1
16	2	31	2				20.4	13.3	21.1
16	2	32	2				21.3	13.7	21.0
16	2	33	2				22.1	14.0	20.9
16	2	34	2				22.8	14.5	20.9
16	2	35	2				23.4	15.0	21.2
16	2	36	2				24.0	15.3	21.0
16	2	37	2				24.5	15.6	21.1
16	2	38	2				25.0	16.0	21.1
16	2	39	2				25.5	16.3	21.1
16	2	40	2				25.9	16.7	21.2
16	2	41	2				26.3	16.9	21.0
16	2	42	2				26.5	17.2	20.8
16	2	43	2				26.9	17.4	20.7
16	2	44	2				27.1	17.6	21.0
16	2	45	2				27.4	17.8	21.0
16	2	46	2				27.6	18.0	21.1
16	2	47	2				27.8	18.2	21.0
16	2	48	2				28.0	18.7	21.0
16	2	49	2				28.2	18.6	21.0
16	2	50	2				28.4	18.8	21.2
16	2	51	2				28.5	18.9	20.9

Table C 46. Continued

16	2	52	2				28.7	19.1	21.0
16	2	53	2				28.9	19.3	21.2
16	2	54	2				29.0	19.4	20.8
16	2	55	2	5	6	0.38	29.1	19.6	21.3
17	1	0	0	0	0	0.29	31.8	26.6	20.6
17	1	1	0				31.9	26.6	21.1
17	1	2	0				32.0	26.7	20.8
17	1	3	0				32.0	26.6	20.9
17	1	4	0				32.1	26.7	21.0
17	1	5	0				32.1	26.7	20.9
17	1	6	1				32.0	26.7	21.1
17	1	7	1				32.0	26.7	20.4
17	1	8	1				32.0	26.7	21.0
17	1	9	1				32.0	26.7	20.8
17	1	10	1				32.0	26.7	20.6
17	1	11	1				32.0	26.7	21.1
17	1	12	1				32.0	26.7	20.9
17	1	13	1				31.9	26.8	21.2
17	1	14	1				31.8	26.7	21.0
17	1	15	1				31.8	26.7	20.7
17	1	16	1				31.7	26.8	20.7
17	1	17	1				31.5	26.7	20.7
17	1	18	1				31.5	26.7	21.0
17	1	19	1				31.4	26.7	20.9
17	1	20	1				31.3	26.8	21.0
17	1	21	1				31.2	26.8	20.9
17	1	22	1				31.1	26.8	20.6
17	1	23	1				30.9	26.8	20.7
17	1	24	1				30.7	26.8	20.9
17	1	25	1	7	63	0.03	30.6	26.8	20.8
17	1	26	2				30.5	26.7	20.5
17	1	27	2				30.3	26.8	21.0
17	1	28	2				30.6	26.9	20.8
17	1	29	2				30.6	26.9	20.7
17	1	30	2				30.4	26.8	20.8
17	1	31	2				30.2	26.8	21.1
17	1	32	2				30.1	26.8	21.2
17	1	33	2				30.0	26.9	21.4
17	1	34	2				30.0	26.9	21.0
17	1	35	2				29.8	26.9	20.6
17	1	36	2				29.7	26.9	20.7
17	1	37	2				29.7	26.9	21.0
17	1	38	2				29.7	26.9	20.8
17	1	39	2				29.6	27.0	20.7
17	1	40	2				29.7	27.0	20.8
17	1	41	2				29.7	27.1	20.8
17	1	42	2				29.6	27.1	20.7

Table C 46. Continued

17	1	43	2				29.5	27.1	20.8
17	1	44	2				29.6	27.1	20.5
17	1	45	2				29.5	27.0	20.6
17	1	46	2				29.5	27.1	20.6
17	1	47	2				29.4	27.2	20.7
17	1	48	2				29.3	27.1	20.9
17	1	49	2				29.4	27.1	20.9
17	1	50	2				29.3	27.1	21.0
17	1	51	2				29.2	27.2	20.8
17	1	52	2				29.4	27.2	20.8
17	1	53	2				29.5	27.3	20.9
17	1	54	2				29.5	27.2	20.8
17	1	55	2	6	19	0.20	29.4	27.3	21.0
18	3	0	0	0	0	0.22	32.5	28.3	20.8
18	3	1	0				32.7	28.5	20.7
18	3	2	0				33.0	28.3	21.1
18	3	3	0				33.1	28.4	20.5
18	3	4	0				33.2	28.5	21.1
18	3	5	0				33.2	28.5	21.0
18	3	6	1				33.3	28.4	20.7
18	3	7	1				33.3	28.5	21.2
18	3	8	1				33.3	28.5	20.5
18	3	9	1				33.4	28.7	20.9
18	3	10	1				33.4	28.6	21.1
18	3	11	1				33.5	28.6	20.7
18	3	12	1				33.5	28.6	20.7
18	3	13	1				33.7	28.6	20.3
18	3	14	1				33.5	28.6	20.6
18	3	15	1				31.0	27.6	21.1
18	3	16	1				31.3	27.8	20.6
18	3	17	1				31.6	27.6	21.0
18	3	18	1				32.0	28.1	21.3
18	3	19	1				32.5	28.1	21.3
18	3	20	1				32.9	28.1	20.5
18	3	21	1				33.2	28.3	21.2
18	3	22	1				33.3	28.3	20.8
18	3	23	1				33.7	28.4	20.8
18	3	24	1				33.9	28.5	20.9
18	3	25	1	30	49	0.10	34.0	28.5	20.8
18	3	26	2				34.2	28.6	21.0
18	3	27	2				34.2	28.7	21.2
18	3	28	2				34.3	28.7	20.9
18	3	29	2				34.3	28.7	20.8
18	3	30	2				34.5	28.8	20.9
18	3	31	2				34.5	28.8	21.0
18	3	32	2				34.6	28.9	20.8
18	3	33	2				34.7	28.8	21.0

Table C 46. Continued

18	3	34	2				32.4	28.2	20.8
18	3	35	2				32.0	28.4	21.3
18	3	36	2				32.3	28.2	20.7
18	3	37	2				32.6	28.2	20.9
18	3	38	2				32.9	28.2	21.2
18	3	39	2				33.1	28.1	20.6
18	3	40	2				33.3	28.2	20.5
18	3	41	2				33.5	28.2	21.1
18	3	42	2				33.6	28.2	20.7
18	3	43	2				33.8	28.2	21.0
18	3	44	2				33.9	28.2	20.6
18	3	45	2				33.9	28.3	21.2
18	3	46	2				34.0	28.3	20.8
18	3	47	2				34.0	28.3	21.1
18	3	48	2				34.1	28.3	20.5
18	3	49	2				34.1	28.3	21.1
18	3	50	2				34.1	28.3	20.9
18	3	51	2				34.2	28.3	21.4
18	3	52	2				34.2	28.3	21.1
18	3	53	2				34.2	28.3	20.3
18	3	54	2				34.2	28.4	20.9
18	3	55	2	5	12	0.11	34.3	28.4	20.7
19	2	0	0	0	0	0.34	34.4	28.8	20.9
19	2	1	0				34.5	28.7	20.8
19	2	2	0				34.4	28.7	21.0
19	2	3	0				34.6	28.7	20.9
19	2	4	0				34.6	28.6	20.7
19	2	5	0				31.7	21.6	21.1
19	2	6	1				21.8	17.3	20.9
19	2	7	1				14.0	16.1	21.0
19	2	8	1				11.0	15.2	21.0
19	2	9	1				9.5	13.4	21.0
19	2	10	1				8.8	12.8	20.8
19	2	11	1				8.4	13.0	21.3
19	2	12	1				8.3	12.4	21.4
19	2	13	1				8.3	12.1	21.2
19	2	14	1				8.2	11.7	20.7
19	2	15	1				8.1	10.4	20.9
19	2	16	1				7.9	10.8	21.0
19	2	17	1				7.8	10.3	20.7
19	2	18	1				7.7	9.9	21.2
19	2	19	1				7.5	9.7	20.9
19	2	20	1				7.4	9.3	21.1
19	2	21	1				7.3	9.0	21.0
19	2	22	1				7.2	8.8	21.1
19	2	23	1				7.2	8.4	21.2
19	2	24	1				7.3	8.1	21.4

Table C 46. Continued

19	2	25	1	10	35	0.38	7.3	8.1	21.4
19	2	26	2				10.9	10.3	21.3
19	2	27	2				13.3	11.5	21.1
19	2	28	2				15.4	12.2	21.4
19	2	29	2				17.1	12.7	21.1
19	2	30	2				18.5	13.1	21.0
19	2	31	2				19.6	13.6	21.4
19	2	32	2				20.5	14.2	21.1
19	2	33	2				21.3	14.7	21.1
19	2	34	2				22.0	15.2	20.7
19	2	35	2				22.6	15.7	21.2
19	2	36	2				23.1	16.2	20.8
19	2	37	2				23.7	16.6	21.2
19	2	38	2				24.1	17.0	21.1
19	2	39	2				24.5	17.4	20.9
19	2	40	2				24.9	17.7	21.0
19	2	41	2				25.3	18.1	21.0
19	2	42	2				25.7	18.3	21.0
19	2	43	2				26.0	18.6	20.8
19	2	44	2				26.4	18.8	20.7
19	2	45	2				26.7	19.1	21.1
19	2	46	2				27.0	19.3	21.4
19	2	47	2				27.3	19.6	21.0
19	2	48	2				27.7	19.8	21.2
19	2	49	2				27.9	20.0	20.8
19	2	50	2				28.1	20.1	21.1
19	2	51	2				28.3	20.3	20.9
19	2	52	2				28.5	20.5	21.0
19	2	53	2				28.7	20.7	21.0
19	2	54	2				28.9	20.9	21.5
19	2	55	2	6	17	0.34	29.0	21.0	21.0
20	1	0	0	0	0	0.26	32.8	29.9	21.7
20	1	1	0				33.0	29.8	21.7
20	1	2	0				33.2	29.8	21.7
20	1	3	0				33.3	29.7	21.5
20	1	4	0				33.5	29.6	21.5
20	1	5	0				33.6	29.5	21.6
20	1	6	1				33.6	29.5	21.5
20	1	7	1				33.6	29.5	21.5
20	1	8	1				33.7	29.5	21.7
20	1	9	1				33.8	29.6	21.7
20	1	10	1				33.8	29.5	21.3
20	1	11	1				33.9	29.5	21.2
20	1	12	1				33.9	29.5	21.4
20	1	13	1				33.9	29.6	21.6
20	1	14	1				33.9	29.4	21.5
20	1	15	1				34.0	29.4	21.6

Table C 46. Continued

20	1	16	1				33.9	29.4	21.2
20	1	17	1				33.9	29.3	21.3
20	1	18	1				33.9	29.3	21.6
20	1	19	1				33.7	29.2	21.5
20	1	20	1				33.4	29.0	21.2
20	1	21	1				33.1	28.8	21.4
20	1	22	1				33.0	28.6	21.4
20	1	23	1				33.0	28.5	21.4
20	1	24	1				33.0	28.3	21.5
20	1	25	1	14	57	0.08	33.1	28.3	21.3
20	1	26	2				33.3	28.2	21.2
20	1	27	2				33.4	28.3	21.5
20	1	28	2				33.5	28.3	21.5
20	1	29	2				33.5	28.3	21.2
20	1	30	2				33.6	28.3	21.3
20	1	31	2				33.6	28.3	21.1
20	1	32	2				33.7	28.4	21.5
20	1	33	2				33.7	28.4	21.4
20	1	34	2				33.7	28.4	21.5
20	1	35	2				33.7	28.5	21.5
20	1	36	2				33.6	28.3	21.6
20	1	37	2				33.6	28.3	21.3
20	1	38	2				33.5	28.3	21.5
20	1	39	2				33.5	28.2	21.4
20	1	40	2				33.5	28.1	21.6
20	1	41	2				33.5	28.2	21.5
20	1	42	2				33.5	28.2	21.4
20	1	43	2				33.5	28.3	21.6
20	1	44	2				33.4	28.3	21.6
20	1	45	2				33.5	28.3	21.3
20	1	46	2				33.5	28.3	21.4
20	1	47	2				33.5	28.3	21.4
20	1	48	2				33.5	28.3	21.5
20	1	49	2				33.5	28.2	21.6
20	1	50	2				33.4	28.2	21.4
20	1	51	2				33.4	28.2	21.2
20	1	52	2				33.4	28.2	21.4
20	1	53	2				33.4	28.1	21.4
20	1	54	2				33.4	28.1	21.5
20	1	55	2	0	2	0.08	33.4	28.2	21.4
21	2	0	0	0	0	0.53	32.5	27.4	21.6
21	2	1	0				32.5	27.4	21.6
21	2	2	0				32.7	27.6	21.7
21	2	3	0				32.7	27.5	21.6
21	2	4	0				32.8	27.5	21.6
21	2	5	0				32.5	27.0	21.7
21	2	6	1				19.9	21.5	21.6

Table C 46. Continued

21	2	7	1				10.0	17.7	21.5
21	2	8	1				7.0	18.3	21.5
21	2	9	1				7.0	17.6	21.7
21	2	10	1				6.1	16.9	21.8
21	2	11	1				5.4	16.3	21.9
21	2	12	1				5.1	16.6	21.7
21	2	13	1				4.9	16.6	21.8
21	2	14	1				4.6	16.0	21.5
21	2	15	1				4.5	15.3	21.5
21	2	16	1				4.3	14.5	21.4
21	2	17	1				4.2	13.9	21.8
21	2	18	1				4.1	13.5	21.7
21	2	19	1				3.7	12.9	21.6
21	2	20	1				3.8	12.5	21.7
21	2	21	1				3.8	12.0	21.5
21	2	22	1				3.7	11.6	21.8
21	2	23	1				3.7	11.1	21.6
21	2	24	1				3.8	10.7	21.4
21	2	25	1	12	40	0.87	5.2	11.4	21.7
21	2	26	2				9.8	13.9	21.7
21	2	27	2				12.5	12.9	21.7
21	2	28	2				14.3	13.0	21.6
21	2	29	2				15.9	13.3	21.5
21	2	30	2				17.3	13.7	21.4
21	2	31	2				18.4	14.1	21.6
21	2	32	2				19.3	14.5	21.5
21	2	33	2				20.1	14.8	21.7
21	2	34	2				20.8	15.2	21.7
21	2	35	2				21.4	15.5	21.5
21	2	36	2				21.9	15.8	21.7
21	2	37	2				22.4	16.1	21.5
21	2	38	2				22.9	16.5	21.5
21	2	39	2				23.3	16.7	21.4
21	2	40	2				23.7	17.0	21.5
21	2	41	2				24.1	17.3	21.4
21	2	42	2				24.4	17.4	21.6
21	2	43	2				24.7	17.7	21.5
21	2	44	2				25.0	18.0	21.4
21	2	45	2				25.3	18.1	21.7
21	2	46	2				25.6	18.3	21.4
21	2	47	2				25.8	18.6	21.4
21	2	48	2				26.1	18.7	21.4
21	2	49	2				26.4	18.9	21.4
21	2	50	2				26.6	19.0	21.7
21	2	51	2				26.8	19.3	21.5
21	2	52	2				26.9	19.4	21.3
21	2	53	2				27.0	19.5	21.4

Table C 46. Continued

21	2	54	2				27.2	19.7	21.7
21	2	55	2	4	10	0.32	27.4	19.9	21.7
22	1	0	0	0	0	0.29	32.8	29.9	21.7
22	1	1	0				33.0	29.8	21.7
22	1	2	0				33.2	29.8	21.7
22	1	3	0				33.3	29.7	21.5
22	1	4	0				33.5	29.6	21.5
22	1	5	0				33.6	29.5	21.6
22	1	6	1				33.6	29.5	21.5
22	1	7	1				33.6	29.5	21.5
22	1	8	1				33.7	29.5	21.7
22	1	9	1				33.8	29.6	21.7
22	1	10	1				33.8	29.5	21.3
22	1	11	1				33.9	29.5	21.2
22	1	12	1				33.9	29.5	21.4
22	1	13	1				33.9	29.6	21.6
22	1	14	1				33.9	29.4	21.5
22	1	15	1				34.0	29.4	21.6
22	1	16	1				33.9	29.4	21.2
22	1	17	1				33.9	29.3	21.3
22	1	18	1				33.9	29.3	21.6
22	1	19	1				33.7	29.2	21.5
22	1	20	1				33.4	29.0	21.2
22	1	21	1				33.1	28.8	21.4
22	1	22	1				33.0	28.6	21.4
22	1	23	1				33.0	28.5	21.4
22	1	24	1				33.0	28.3	21.5
22	1	25	1	12	17	0.14	33.1	28.3	21.3
22	1	26	2				33.3	28.2	21.2
22	1	27	2				33.4	28.3	21.5
22	1	28	2				33.5	28.3	21.5
22	1	29	2				33.5	28.3	21.2
22	1	30	2				33.6	28.3	21.3
22	1	31	2				33.6	28.3	21.1
22	1	32	2				33.7	28.4	21.5
22	1	33	2				33.7	28.4	21.4
22	1	34	2				33.7	28.4	21.5
22	1	35	2				33.7	28.5	21.5
22	1	36	2				33.6	28.3	21.6
22	1	37	2				33.6	28.3	21.3
22	1	38	2				33.5	28.3	21.5
22	1	39	2				33.5	28.2	21.4
22	1	40	2				33.5	28.1	21.6
22	1	41	2				33.5	28.2	21.5
22	1	42	2				33.5	28.2	21.4
22	1	43	2				33.5	28.3	21.6
22	1	44	2				33.4	28.3	21.6

Table C 46. Continued

22	1	45	2				33.5	28.3	21.3
22	1	46	2				33.5	28.3	21.4
22	1	47	2				33.5	28.3	21.4
22	1	48	2				33.5	28.3	21.5
22	1	49	2				33.5	28.2	21.6
22	1	50	2				33.4	28.2	21.4
22	1	51	2				33.4	28.2	21.2
22	1	52	2				33.4	28.2	21.4
22	1	53	2				33.4	28.1	21.4
22	1	54	2				33.4	28.1	21.5
22	1	55	2	2	3	0.08	33.4	28.2	21.4
23	3	0	0	0	0	0.81	32.9	27.1	21.5
23	3	1	0				33.2	27.9	21.4
23	3	2	0				33.4	27.6	21.5
23	3	3	0				33.5	27.9	21.5
23	3	4	0				33.6	28.0	21.7
23	3	5	0				33.6	28.0	21.5
23	3	6	1				33.7	28.0	21.6
23	3	7	1				33.8	28.0	21.8
23	3	8	1				33.9	27.8	21.4
23	3	9	1				33.9	27.9	21.5
23	3	10	1				33.9	27.9	21.4
23	3	11	1				32.7	27.4	21.5
23	3	12	1				33.2	28.1	21.4
23	3	13	1				32.9	28.1	21.5
23	3	14	1				33.0	28.2	21.6
23	3	15	1				33.1	28.2	21.3
23	3	16	1				33.2	28.2	21.7
23	3	17	1				33.4	28.3	21.7
23	3	18	1				33.6	28.3	21.6
23	3	19	1				33.8	28.3	21.6
23	3	20	1				33.9	28.4	21.6
23	3	21	1				34.0	28.4	21.7
23	3	22	1				34.1	28.5	21.3
23	3	23	1				34.2	28.5	21.5
23	3	24	1				34.3	28.6	21.5
23	3	25	1	7	3	0.73	34.4	28.6	21.6
23	3	26	2				34.4	28.7	21.7
23	3	27	2				34.5	28.7	21.8
23	3	28	2				34.6	28.8	21.7
23	3	29	2				34.7	28.8	21.5
23	3	30	2				33.2	28.3	21.4
23	3	31	2				33.3	28.2	21.6
23	3	32	2				33.8	28.3	21.5
23	3	33	2				34.1	28.4	21.8
23	3	34	2				34.3	28.4	21.7
23	3	35	2				34.4	28.4	21.6

Table C 46. Continued

23	3	36	2				34.6	28.3	21.5
23	3	37	2				34.6	28.3	21.6
23	3	38	2				34.7	28.3	21.6
23	3	39	2				34.8	28.3	21.6
23	3	40	2				34.8	28.3	21.5
23	3	41	2				34.8	28.3	21.5
23	3	42	2				34.9	28.2	21.6
23	3	43	2				34.9	28.1	21.5
23	3	44	2				34.9	28.1	21.7
23	3	45	2				34.9	28.1	21.6
23	3	46	2				34.9	28.1	21.4
23	3	47	2				35.0	28.1	21.5
23	3	48	2				35.0	28.0	21.7
23	3	49	2				35.0	28.0	21.6
23	3	50	2				35.0	28.0	21.4
23	3	51	2				35.0	28.1	21.5
23	3	52	2				35.0	28.1	21.5
23	3	53	2				35.0	28.0	21.5
23	3	54	2				35.1	28.0	21.6
23	3	55	2	5	1	0.82	35.1	28.0	21.6
24	4	0	0	0	0	0.37	32.9	29.3	21.8
24	4	1	0				33.0	29.7	21.6
24	4	2	0				33.0	29.7	21.8
24	4	3	0				33.0	29.5	21.1
24	4	4	0				33.1	29.6	21.6
24	4	5	0				33.2	29.5	21.6
24	4	6	1				33.2	29.3	21.6
24	4	7	1				33.2	29.4	21.3
24	4	8	1				33.2	29.3	21.3
24	4	9	1				33.2	29.2	21.5
24	4	10	1				33.3	29.2	21.4
24	4	11	1				33.3	29.2	21.6
24	4	12	1				33.3	29.2	21.6
24	4	13	1				33.3	29.1	21.5
24	4	14	1				33.3	29.0	21.5
24	4	15	1				33.3	29.0	21.4
24	4	16	1				33.3	29.0	21.5
24	4	17	1				33.3	28.9	21.4
24	4	18	1				33.3	29.0	21.5
24	4	19	1				33.3	28.9	21.6
24	4	20	1				33.3	28.9	21.5
24	4	21	1				33.3	28.8	21.6
24	4	22	1				33.3	28.5	21.6
24	4	23	1				33.3	28.6	21.6
24	4	24	1				33.3	28.4	21.7
24	4	25	1	0	0	0.38	33.2	28.6	21.5
24	4	26	2				33.2	28.6	21.5

Table C 46. Continued

24	4	27	2				33.2	28.6	21.9
24	4	28	2				33.2	28.6	21.5
24	4	29	2				33.2	28.6	21.5
24	4	30	2				33.2	28.5	21.5
24	4	31	2				33.2	28.5	21.7
24	4	32	2				33.2	28.4	21.5
24	4	33	2				33.2	28.5	21.0
24	4	34	2				33.2	28.3	21.3
24	4	35	2				33.2	28.5	21.5
24	4	36	2				33.2	28.4	21.6
24	4	37	2				33.2	28.5	21.4
24	4	38	2				33.2	28.4	21.6
24	4	39	2				33.1	28.4	21.4
24	4	40	2				33.1	28.4	21.4
24	4	41	2				33.1	28.4	21.6
24	4	42	2				33.1	28.4	21.3
24	4	43	2				33.1	28.4	21.6
24	4	44	2				33.1	28.4	21.7
24	4	45	2				33.0	28.4	21.5
24	4	46	2				33.1	28.3	21.6
24	4	47	2				33.0	28.3	21.5
24	4	48	2				33.0	28.0	21.5
24	4	49	2				33.0	28.4	21.5
24	4	50	2				33.0	28.4	21.6
24	4	51	2				33.0	28.3	21.6
24	4	52	2				33.0	28.3	21.6
24	4	53	2				33.0	28.4	21.6
24	4	54	2				33.0	28.3	21.6
24	4	55	2	0	1	0.40	33.0	28.3	21.6
25	2	0	0	0	0	0.19	32.3	28.2	21.8
25	2	1	0				32.4	28.2	21.7
25	2	2	0				32.5	28.2	21.5
25	2	3	0				32.6	28.4	21.7
25	2	4	0				32.7	28.3	21.5
25	2	5	0				32.3	28.1	21.4
25	2	6	1				24.5	25.2	21.3
25	2	7	1				14.1	23.1	21.6
25	2	8	1				10.0	21.1	21.8
25	2	9	1				7.8	19.5	21.5
25	2	10	1				6.8	17.4	21.7
25	2	11	1				6.1	15.8	21.5
25	2	12	1				5.7	14.6	21.5
25	2	13	1				5.4	13.6	21.6
25	2	14	1				5.3	12.8	21.6
25	2	15	1				5.3	12.0	21.4
25	2	16	1				5.3	11.5	21.5
25	2	17	1				5.4	10.9	21.4

Table C 46. Continued

25	2	18	1				5.5	10.4	21.7
25	2	19	1				5.5	9.9	21.6
25	2	20	1				5.4	9.5	21.4
25	2	21	1				5.5	9.1	21.6
25	2	22	1				5.5	8.8	21.5
25	2	23	1				5.6	8.4	21.4
25	2	24	1				5.5	8.2	21.6
25	2	25	1	10	16	0.31	5.4	8.0	21.4
25	2	26	2				10.0	9.6	21.7
25	2	27	2				12.4	10.4	21.8
25	2	28	2				14.5	11.1	21.7
25	2	29	2				16.3	12.0	21.5
25	2	30	2				17.9	13.2	21.5
25	2	31	2				19.2	14.1	21.6
25	2	32	2				20.4	15.1	21.7
25	2	33	2				21.4	15.9	21.6
25	2	34	2				22.4	16.8	21.5
25	2	35	2				23.1	17.5	21.5
25	2	36	2				23.9	18.0	21.5
25	2	37	2				24.5	18.4	21.5
25	2	38	2				25.1	18.8	21.7
25	2	39	2				25.6	19.1	21.8
25	2	40	2				26.0	19.3	21.6
25	2	41	2				26.4	19.5	21.5
25	2	42	2				26.8	19.6	21.4
25	2	43	2				27.2	19.7	21.4
25	2	44	2				27.5	19.8	21.6
25	2	45	2				27.8	19.9	21.7
25	2	46	2				28.0	20.1	21.4
25	2	47	2				28.2	20.2	21.6
25	2	48	2				28.5	20.3	21.3
25	2	49	2				28.7	20.4	21.6
25	2	50	2				28.9	20.5	21.4
25	2	51	2				29.1	20.7	21.5
25	2	52	2				29.3	20.8	21.5
25	2	53	2				29.4	20.9	21.4
25	2	54	2				29.6	21.0	21.4
25	2	55	2	1	16	0.27	29.7	21.1	21.5
26	2	0	0	0	0	0.44	31.7	27.4	21.2
26	2	1	0				31.8	27.4	20.8
26	2	2	0				31.9	27.5	20.8
26	2	3	0				31.8	27.6	20.4
26	2	4	0				31.8	27.3	20.9
26	2	5	0				23.1	24.6	21.2
26	2	6	1				18.0	23.6	21.1
26	2	7	1				13.6	22.2	20.6
26	2	8	1				10.9	21.4	20.7

Table C 46. Continued

26	2	9	1				9.0	19.3	20.8
26	2	10	1				7.8	16.6	20.8
26	2	11	1				6.8	15.4	20.5
26	2	12	1				6.2	14.5	20.7
26	2	13	1				5.6	13.7	20.7
26	2	14	1				5.2	13.1	20.8
26	2	15	1				4.8	12.4	20.6
26	2	16	1				4.5	12.0	20.5
26	2	17	1				4.2	11.6	20.3
26	2	18	1				4.0	11.1	20.1
26	2	19	1				3.9	10.8	20.7
26	2	20	1				3.8	10.4	20.6
26	2	21	1				3.8	10.1	20.5
26	2	22	1				3.8	9.8	20.6
26	2	23	1				3.8	9.5	20.6
26	2	24	1				3.8	9.3	20.7
26	2	25	1	10	31	0.69	6.8	11.8	20.6
26	2	26	2				9.1	12.3	21.0
26	2	27	2				10.8	12.8	20.7
26	2	28	2				12.3	13.3	20.4
26	2	29	2				13.7	13.7	21.1
26	2	30	2				15.0	14.3	20.9
26	2	31	2				16.0	14.7	20.4
26	2	32	2				17.1	15.1	20.7
26	2	33	2				18.0	15.4	20.7
26	2	34	2				18.9	15.9	20.6
26	2	35	2				19.9	16.2	20.6
26	2	36	2				20.8	16.6	20.6
26	2	37	2				21.8	17.0	20.6
26	2	38	2				22.7	17.6	20.8
26	2	39	2				23.4	18.1	20.7
26	2	40	2				24.1	18.8	20.6
26	2	41	2				24.6	19.8	20.5
26	2	42	2				25.0	20.9	20.6
26	2	43	2				25.3	22.3	20.7
26	2	44	2				25.7	23.6	20.8
26	2	45	2				26.0	24.9	20.8
26	2	46	2				26.3	26.0	20.5
26	2	47	2				26.6	26.9	20.6
26	2	48	2				26.9	27.5	20.8
26	2	49	2				27.1	27.8	20.6
26	2	50	2				27.3	28.1	20.7
26	2	51	2				27.5	28.0	20.5
26	2	52	2				27.6	28.1	20.5
26	2	53	2				27.8	28.1	20.6
26	2	54	2				27.9	28.0	20.6
26	2	55	2	4	15	0.69	28.0	27.9	21.1

Table C 46. Continued

27	3	0	0	0	0	0.26	31.6	28.1	21.5
27	3	1	0				31.7	28.2	21.4
27	3	2	0				31.6	28.3	21.4
27	3	3	0				31.7	28.4	21.4
27	3	4	0				31.8	28.3	21.4
27	3	5	0				31.9	28.4	21.5
27	3	6	1				32.0	28.3	21.4
27	3	7	1				32.0	28.4	21.3
27	3	8	1				32.1	28.3	21.3
27	3	9	1				32.1	28.4	21.5
27	3	10	1				32.1	28.4	21.4
27	3	11	1				32.2	28.6	21.5
27	3	12	1				32.4	28.5	21.4
27	3	13	1				32.4	28.6	21.5
27	3	14	1				32.5	28.6	21.7
27	3	15	1				32.5	28.6	21.2
27	3	16	1				32.5	28.7	21.4
27	3	17	1				32.6	28.6	21.4
27	3	18	1				31.7	27.2	21.6
27	3	19	1				30.4	28.0	21.7
27	3	20	1				30.4	28.1	21.5
27	3	21	1				30.6	28.1	21.4
27	3	22	1				30.7	28.1	21.5
27	3	23	1				30.9	28.1	21.2
27	3	24	1				31.0	28.1	21.3
27	3	25	1	17	62	0.20	31.2	28.2	21.6
27	3	26	2				31.3	28.2	21.5
27	3	27	2				31.4	28.2	21.4
27	3	28	2				31.5	28.3	21.7
27	3	29	2				31.6	28.3	21.3
27	3	30	2				31.6	28.4	21.4
27	3	31	2				31.7	28.4	21.5
27	3	32	2				31.8	28.4	21.5
27	3	33	2				31.9	28.5	21.2
27	3	34	2				31.9	28.5	21.4
27	3	35	2				32.0	28.5	21.5
27	3	36	2				32.1	28.6	21.4
27	3	37	2				32.0	28.6	21.6
27	3	38	2				31.3	28.5	21.6
27	3	39	2				31.5	29.4	21.6
27	3	40	2				31.8	30.0	21.3
27	3	41	2				32.0	30.2	21.5
27	3	42	2				32.0	30.4	21.4
27	3	43	2				32.2	30.4	21.1
27	3	44	2				32.4	30.3	21.0
27	3	45	2				32.5	30.4	21.5
27	3	46	2				32.6	30.6	21.5

Table C 46. Continued

27	3	47	2				32.6	30.6	21.3
27	3	48	2				32.7	30.6	21.4
27	3	49	2				32.8	30.7	21.2
27	3	50	2				32.8	30.7	21.5
27	3	51	2				32.9	30.8	21.3
27	3	52	2				32.9	30.8	21.2
27	3	53	2				33.0	30.9	21.5
27	3	54	2				33.0	30.9	21.4
27	3	55	2	16	22	0.19	33.1	30.9	21.5
28	1	0	0	0	0	0.34	33.4	27.2	20.7
28	1	1	0				33.5	27.2	20.8
28	1	2	0				33.5	27.4	21.1
28	1	3	0				33.5	27.2	20.8
28	1	4	0				33.6	27.2	21.0
28	1	5	0				33.7	27.2	21.0
28	1	6	1				33.7	27.2	21.1
28	1	7	1				33.7	27.1	21.1
28	1	8	1				33.8	27.0	20.9
28	1	9	1				33.8	27.0	20.9
28	1	10	1				33.9	27.1	21.2
28	1	11	1				34.0	27.0	21.0
28	1	12	1				34.0	27.0	21.0
28	1	13	1				34.0	27.1	21.1
28	1	14	1				34.0	26.9	20.5
28	1	15	1				34.0	27.0	21.0
28	1	16	1				34.0	27.0	21.2
28	1	17	1				34.0	27.1	21.2
28	1	18	1				34.1	27.0	20.9
28	1	19	1				34.1	27.0	20.9
28	1	20	1				34.0	26.8	21.2
28	1	21	1				33.9	27.0	21.0
28	1	22	1				33.8	26.8	20.9
28	1	23	1				33.7	26.8	20.8
28	1	24	1				33.7	26.9	21.0
28	1	25	1	7	24	0.12	33.6	26.7	20.5
28	1	26	2				33.5	26.6	21.1
28	1	27	2				33.5	26.9	20.7
28	1	28	2				33.5	27.0	20.3
28	1	29	2				33.6	27.0	20.8
28	1	30	2				33.6	26.9	21.1
28	1	31	2				33.6	27.0	21.1
28	1	32	2				33.7	26.9	21.0
28	1	33	2				33.7	26.9	20.3
28	1	34	2				33.7	27.0	20.8
28	1	35	2				33.7	26.9	21.0
28	1	36	2				33.7	27.0	21.0
28	1	37	2				33.7	27.0	20.9

Table C 46. Continued

28	1	38	2				33.6	27.2	20.6
28	1	39	2				33.6	27.2	20.6
28	1	40	2				33.6	27.1	21.0
28	1	41	2				33.6	27.2	20.7
28	1	42	2				33.6	27.1	21.0
28	1	43	2				33.6	27.2	20.9
28	1	44	2				33.5	27.1	20.9
28	1	45	2				33.5	27.2	21.0
28	1	46	2				33.5	27.2	21.0
28	1	47	2				33.6	27.1	21.2
28	1	48	2				33.5	27.0	20.8
28	1	49	2				33.5	27.3	20.7
28	1	50	2				33.5	27.3	20.7
28	1	51	2				33.4	27.4	20.8
28	1	52	2				33.4	27.4	21.0
28	1	53	2				33.3	27.3	20.6
28	1	54	2				33.3	27.5	20.9
28	1	55	2	0	0	0.11	33.3	27.3	20.6
29	3	0	0	0	0	0.29	31.8	28.4	20.6
29	3	1	0				32.0	28.5	21.1
29	3	2	0				32.1	28.5	21.0
29	3	3	0				32.2	28.6	21.1
29	3	4	0				32.4	28.6	21.1
29	3	5	0				32.5	28.7	21.1
29	3	6	1				32.6	28.6	20.9
29	3	7	1				32.6	28.7	20.8
29	3	8	1				32.7	28.6	20.9
29	3	9	1				30.3	27.9	21.1
29	3	10	1				30.6	28.2	21.1
29	3	11	1				30.6	27.9	21.0
29	3	12	1				30.7	27.9	20.6
29	3	13	1				30.7	27.9	20.6
29	3	14	1				30.8	27.9	21.1
29	3	15	1				30.9	27.8	21.2
29	3	16	1				31.0	27.8	20.9
29	3	17	1				31.1	27.8	20.8
29	3	18	1				31.1	27.8	21.1
29	3	19	1				31.2	27.9	21.1
29	3	20	1				31.3	27.8	20.8
29	3	21	1				31.4	27.9	21.1
29	3	22	1				31.4	27.9	20.7
29	3	23	1				31.5	27.9	20.9
29	3	24	1				31.6	27.9	20.6
29	3	25	1	25	62	0.04	31.6	28.0	20.7
29	3	26	2				31.7	28.0	20.9
29	3	27	2				31.7	28.0	21.0
29	3	28	2				31.4	27.8	21.0

Table C 46. Continued

29	3	29	2				31.2	27.9	21.0
29	3	30	2				31.3	27.9	20.9
29	3	31	2				31.3	28.0	21.0
29	3	32	2				31.4	28.1	20.9
29	3	33	2				31.4	28.1	21.1
29	3	34	2				31.4	28.2	20.7
29	3	35	2				31.5	28.1	21.3
29	3	36	2				31.5	28.2	20.7
29	3	37	2				31.6	28.1	21.3
29	3	38	2				31.6	28.2	21.0
29	3	39	2				31.7	28.2	20.8
29	3	40	2				31.7	28.2	20.9
29	3	41	2				31.7	28.1	20.6
29	3	42	2				31.8	28.3	20.7
29	3	43	2				31.8	28.3	20.9
29	3	44	2				31.8	28.3	20.8
29	3	45	2				31.8	28.4	20.6
29	3	46	2				31.9	28.4	20.8
29	3	47	2				31.9	28.4	20.9
29	3	48	2				31.9	28.4	21.0
29	3	49	2				31.9	28.5	20.8
29	3	50	2				32.0	28.5	20.7
29	3	51	2				32.0	28.5	20.8
29	3	52	2				32.0	28.5	20.6
29	3	53	2				32.0	28.5	20.9
29	3	54	2				32.1	28.5	20.9
29	3	55	2	4	8	0.20	32.1	28.6	21.0
30	1	0	0	0	0	0.78	33.7	28.9	21.2
30	1	1	0				33.8	29.2	20.6
30	1	2	0				33.8	29.2	20.2
30	1	3	0				33.9	29.3	20.3
30	1	4	0				33.9	29.3	20.4
30	1	5	0				34.2	29.4	20.2
30	1	6	1				34.2	29.4	20.3
30	1	7	1				34.1	29.4	20.4
30	1	8	1				34.1	29.3	20.6
30	1	9	1				34.0	29.4	20.7
30	1	10	1				34.1	29.4	21.1
30	1	11	1				34.1	29.5	20.9
30	1	12	1				34.1	29.6	20.6
30	1	13	1				34.2	29.6	20.8
30	1	14	1				34.3	29.7	20.8
30	1	15	1				34.3	29.6	20.5
30	1	16	1				34.0	29.7	20.7
30	1	17	1				34.0	29.7	20.5
30	1	18	1				34.0	29.6	21.1
30	1	19	1				34.1	29.5	21.2

Table C 46. Continued

30	1	20	1				34.2	29.5	20.7
30	1	21	1				34.2	29.5	21.0
30	1	22	1				34.3	29.4	21.0
30	1	23	1				34.3	29.5	21.0
30	1	24	1				34.4	29.5	20.8
30	1	25	1	16	63	0.66	34.3	29.4	20.8
30	1	26	2				34.4	29.5	20.8
30	1	27	2				34.3	29.5	21.2
30	1	28	2				34.3	29.6	21.1
30	1	29	2				34.3	29.5	20.7
30	1	30	2				34.3	29.5	20.5
30	1	31	2				34.2	29.7	20.6
30	1	32	2				34.2	29.8	20.6
30	1	33	2				33.9	30.1	21.1
30	1	34	2				33.9	30.2	21.2
30	1	35	2				34.0	30.2	21.1
30	1	36	2				34.0	30.3	21.2
30	1	37	2				34.0	30.5	20.8
30	1	38	2				34.2	30.8	20.4
30	1	39	2				34.3	30.9	20.5
30	1	40	2				34.5	30.9	20.3
30	1	41	2				34.6	31.2	20.7
30	1	42	2				34.7	31.1	20.8
30	1	43	2				34.6	31.3	20.6
30	1	44	2				34.4	31.4	20.3
30	1	45	2				34.4	31.5	20.7
30	1	46	2				34.6	31.6	20.6
30	1	47	2				34.6	31.8	20.5
30	1	48	2				34.6	31.7	21.0
30	1	49	2				34.6	31.8	20.8
30	1	50	2				34.6	31.8	20.2
30	1	51	2				34.6	31.8	20.4
30	1	52	2				34.7	31.8	20.7
30	1	53	2				34.8	31.9	20.6
30	1	54	2				34.9	32.0	20.6
30	1	55	2	11	28	0.61	35.0	31.9	21.0
31	4	0	0	0	0	0.97	32.2	26.8	21.7
31	4	1	0				32.3	25.4	21.9
31	4	2	0				32.3	25.5	21.9
31	4	3	0				32.3	25.3	21.8
31	4	4	0				32.3	25.3	21.8
31	4	5	0				32.3	25.4	21.9
31	4	6	1				32.3	25.3	21.9
31	4	7	1				32.3	25.3	21.7
31	4	8	1				32.3	25.2	21.7
31	4	9	1				32.3	25.3	21.8
31	4	10	1				32.4	25.1	21.8

Table C 46. Continued

31	4	11	1				30.7	26.5	21.6
31	4	12	1				31.7	26.6	21.7
31	4	13	1				31.6	26.7	21.9
31	4	14	1				31.6	26.7	21.9
31	4	15	1				31.5	26.7	21.9
31	4	16	1				31.4	26.7	21.8
31	4	17	1				31.4	26.7	21.9
31	4	18	1				31.4	26.8	21.9
31	4	19	1				31.4	26.8	21.9
31	4	20	1				31.4	26.8	21.9
31	4	21	1				31.4	26.8	21.9
31	4	22	1				31.4	26.8	21.8
31	4	23	1				31.5	26.8	22.0
31	4	24	1				31.5	26.8	22.0
31	4	25	1	0	0	0.97	31.5	26.8	21.9
31	4	26	2				31.6	26.8	21.9
31	4	27	2				31.6	26.8	21.9
31	4	28	2				31.6	26.8	21.8
31	4	29	2				31.7	26.9	21.9
31	4	30	2				31.7	26.8	22.0
31	4	31	2				31.8	26.8	21.9
31	4	32	2				31.8	26.9	21.8
31	4	33	2				31.9	26.9	21.8
31	4	34	2				31.9	26.9	21.9
31	4	35	2				31.9	26.9	21.9
31	4	36	2				32.0	26.9	21.8
31	4	37	2				32.0	26.9	22.0
31	4	38	2				32.1	27.0	22.0
31	4	39	2				32.1	26.9	21.9
31	4	40	2				32.1	26.9	21.9
31	4	41	2				32.2	27.0	22.0
31	4	42	2				32.2	27.0	21.8
31	4	43	2				32.2	27.0	22.0
31	4	44	2				32.3	27.0	22.0
31	4	45	2				32.3	27.0	21.9
31	4	46	2				32.4	27.0	21.8
31	4	47	2				32.4	27.0	21.8
31	4	48	2				32.4	27.0	21.9
31	4	49	2				32.5	27.1	22.0
31	4	50	2				32.5	27.0	21.8
31	4	51	2				32.1	26.8	21.9
31	4	52	2				32.1	26.6	21.9
31	4	53	2				32.1	26.5	21.9
31	4	54	2				32.2	26.5	21.9
31	4	55	2	0	0	0.97	32.2	26.5	21.9
32	1	0	0	0	0	0.18	33.3	27.3	20.5
32	1	1	0				33.4	27.4	20.9

Table C 46. Continued

32	1	2	0				33.4	27.5	20.6
32	1	3	0				33.5	27.5	20.6
32	1	4	0				33.6	27.5	20.9
32	1	5	0				33.6	27.5	21.0
32	1	6	1				33.7	27.6	20.5
32	1	7	1				33.8	27.6	20.7
32	1	8	1				33.8	27.7	20.2
32	1	9	1				33.9	27.6	20.6
32	1	10	1				33.9	27.6	20.8
32	1	11	1				33.9	27.6	20.7
32	1	12	1				34.0	27.9	20.6
32	1	13	1				34.0	27.8	20.5
32	1	14	1				34.0	27.9	20.5
32	1	15	1				34.0	27.9	20.6
32	1	16	1				34.0	27.9	20.6
32	1	17	1				34.0	27.9	21.0
32	1	18	1				34.0	27.9	20.8
32	1	19	1				34.0	28.0	21.0
32	1	20	1				34.0	28.0	20.9
32	1	21	1				34.0	28.1	20.2
32	1	22	1				34.0	28.1	20.4
32	1	23	1				34.1	28.1	20.5
32	1	24	1				34.1	28.3	20.5
32	1	25	1	23	30	0.09	34.1	28.3	20.3
32	1	26	2				34.1	28.4	20.5
32	1	27	2				34.1	28.4	20.8
32	1	28	2				34.1	28.5	20.4
32	1	29	2				34.0	28.6	20.3
32	1	30	2				33.9	28.7	20.5
32	1	31	2				33.7	28.6	20.7
32	1	32	2				33.7	28.6	20.5
32	1	33	2				33.7	28.7	20.8
32	1	34	2				33.5	28.7	21.1
32	1	35	2				33.5	28.7	21.3
32	1	36	2				33.5	28.7	20.7
32	1	37	2				33.5	28.7	20.6
32	1	38	2				33.5	28.9	20.8
32	1	39	2				33.4	28.8	20.9
32	1	40	2				33.5	28.8	20.5
32	1	41	2				33.5	29.0	20.9
32	1	42	2				33.6	29.1	20.6
32	1	43	2				33.7	29.2	20.5
32	1	44	2				33.7	29.2	20.5
32	1	45	2				33.8	29.3	20.6
32	1	46	2				33.8	29.4	20.4
32	1	47	2				33.9	29.5	20.6
32	1	48	2				33.9	29.6	20.8

Table C 46. Continued

32	1	49	2				33.9	29.7	20.8
32	1	50	2				33.9	29.8	20.5
32	1	51	2				33.9	30.0	20.6
32	1	52	2				33.9	30.0	20.4
32	1	53	2				33.9	30.3	20.5
32	1	54	2				34.0	30.5	20.6
32	1	55	2	2	1	0.06	34.0	30.7	20.7
33	3	0	0	0	0	0.31	32.3	27.9	21.2
33	3	1	0				32.5	28.0	21.3
33	3	2	0				32.6	28.1	21.0
33	3	3	0				32.7	28.0	20.8
33	3	4	0				32.9	28.2	21.0
33	3	5	0				33.0	28.1	20.7
33	3	6	1				33.1	28.2	21.0
33	3	7	1				33.1	27.9	20.9
33	3	8	1				33.2	28.3	20.8
33	3	9	1				31.7	26.8	21.2
33	3	10	1				33.3	27.0	21.2
33	3	11	1				33.1	27.0	21.3
33	3	12	1				33.0	27.1	21.2
33	3	13	1				33.0	27.2	20.9
33	3	14	1				33.0	27.3	20.8
33	3	15	1				32.9	27.3	21.0
33	3	16	1				33.0	27.3	21.1
33	3	17	1				33.0	27.4	21.1
33	3	18	1				33.0	27.5	20.8
33	3	19	1				33.0	27.5	20.8
33	3	20	1				33.1	27.6	20.8
33	3	21	1				33.2	27.7	20.9
33	3	22	1				33.3	27.8	21.3
33	3	23	1				33.4	27.9	20.8
33	3	24	1				33.4	28.0	21.1
33	3	25	1	16	61	0.15	33.5	28.1	21.1
33	3	26	2				33.5	28.2	21.0
33	3	27	2				33.5	28.3	21.0
33	3	28	2				33.5	28.4	21.3
33	3	29	2				33.6	28.5	21.1
33	3	30	2				33.6	28.7	20.9
33	3	31	2				32.6	28.6	21.1
33	3	32	2				32.6	28.7	21.2
33	3	33	2				32.8	28.8	21.1
33	3	34	2				32.9	28.8	21.2
33	3	35	2				33.0	28.9	21.3
33	3	36	2				33.1	29.0	21.0
33	3	37	2				33.2	29.1	21.0
33	3	38	2				33.3	29.2	21.1
33	3	39	2				33.4	29.4	21.1

Table C 46. Continued

33	3	40	2				33.5	29.4	20.7
33	3	41	2				33.5	29.6	21.0
33	3	42	2				33.6	29.6	21.2
33	3	43	2				33.7	29.5	21.0
33	3	44	2				33.8	29.7	20.6
33	3	45	2				33.9	29.7	21.0
33	3	46	2				33.9	29.8	21.0
33	3	47	2				34.0	30.1	21.0
33	3	48	2				34.0	30.1	20.8
33	3	49	2				34.0	30.2	21.0
33	3	50	2				34.0	30.2	21.1
33	3	51	2				34.0	30.2	21.1
33	3	52	2				34.0	30.2	21.0
33	3	53	2				34.1	30.2	20.9
33	3	54	2				34.1	30.3	21.0
33	3	55	2	10	48	0.16	34.1	30.3	20.5
34	2	0	0	0	0	0.38	31.1	27.0	21.0
34	2	1	0				31.2	27.1	20.9
34	2	2	0				31.2	27.0	21.1
34	2	3	0				31.3	27.1	21.2
34	2	4	0				31.3	27.1	20.3
34	2	5	0				31.4	27.1	21.3
34	2	6	1				22.3	12.9	21.3
34	2	7	1				15.7	11.4	21.1
34	2	8	1				13.5	8.8	21.0
34	2	9	1				11.3	7.3	20.8
34	2	10	1				10.4	6.5	20.7
34	2	11	1				9.9	5.8	20.8
34	2	12	1				9.1	5.2	20.8
34	2	13	1				8.9	4.7	20.7
34	2	14	1				8.5	4.4	21.0
34	2	15	1				8.1	4.2	20.7
34	2	16	1				7.7	4.0	20.8
34	2	17	1				7.7	3.9	20.6
34	2	18	1				7.3	3.8	20.6
34	2	19	1				7.1	3.6	20.9
34	2	20	1				7.1	3.4	20.4
34	2	21	1				7.0	3.3	20.7
34	2	22	1				6.9	3.2	20.7
34	2	23	1				6.8	3.1	20.7
34	2	24	1				7.0	3.0	20.3
34	2	25	1	10	15	0.57	7.0	3.0	20.6
34	2	26	2				12.9	6.2	21.0
34	2	27	2				15.2	7.2	21.2
34	2	28	2				16.8	8.0	21.4
34	2	29	2				18.1	8.8	21.3
34	2	30	2				19.1	9.5	21.0

Table C 46. Continued

34	2	31	2				19.9	10.2	21.0
34	2	32	2				20.6	10.8	20.3
34	2	33	2				21.2	11.5	20.9
34	2	34	2				21.7	12.0	20.7
34	2	35	2				22.2	12.5	20.7
34	2	36	2				22.5	13.1	20.5
34	2	37	2				22.9	13.6	21.1
34	2	38	2				23.2	13.9	20.9
34	2	39	2				23.5	14.3	20.5
34	2	40	2				23.7	14.6	20.7
34	2	41	2				24.1	14.8	20.8
34	2	42	2				24.4	15.2	20.5
34	2	43	2				24.6	15.4	20.7
34	2	44	2				24.8	15.7	21.1
34	2	45	2				25.0	16.0	20.8
34	2	46	2				25.2	16.2	20.7
34	2	47	2				25.4	16.4	20.5
34	2	48	2				25.6	16.5	20.7
34	2	49	2				25.7	16.8	20.5
34	2	50	2				25.9	16.9	20.5
34	2	51	2				26.1	17.1	21.0
34	2	52	2				26.3	17.3	20.8
34	2	53	2				26.4	17.5	20.6
34	2	54	2				26.5	17.6	20.8
34	2	55	2	1	2	0.13	26.7	17.7	20.6
35	4	0	0	1	0	0.12	34.9	27.3	22.0
35	4	1	0				34.9	27.2	22.0
35	4	2	0				34.9	27.3	21.9
35	4	3	0				35.0	27.2	22.1
35	4	4	0				35.0	27.0	21.9
35	4	5	0				35.0	27.2	22.1
35	4	6	1				35.0	27.2	22.0
35	4	7	1				35.1	27.1	22.1
35	4	8	1				35.1	27.1	22.0
35	4	9	1				35.0	27.0	21.9
35	4	10	1				35.1	27.0	18.2
35	4	11	1				35.0	27.0	22.1
35	4	12	1				35.1	26.9	22.0
35	4	13	1				33.9	26.8	21.8
35	4	14	1				34.3	26.7	22.0
35	4	15	1				34.7	26.7	22.0
35	4	16	1				34.9	26.6	22.0
35	4	17	1				35.1	26.7	22.0
35	4	18	1				35.2	26.6	21.9
35	4	19	1				35.3	26.7	22.1
35	4	20	1				35.4	26.7	22.0
35	4	21	1				35.5	26.7	22.0

Table C 46. Continued

35	4	22	1				35.5	26.7	22.0
35	4	23	1				35.5	26.7	22.1
35	4	24	1				35.5	26.7	22.0
35	4	25	1	0	0	0.12	35.6	26.8	22.0
35	4	26	2				35.6	26.8	22.0
35	4	27	2				35.6	26.8	22.0
35	4	28	2				35.6	26.8	22.0
35	4	29	2				35.6	26.8	22.0
35	4	30	2				35.7	26.9	22.1
35	4	31	2				35.7	26.9	22.1
35	4	32	2				35.7	26.9	22.0
35	4	33	2				35.7	26.9	22.0
35	4	34	2				35.7	26.9	22.1
35	4	35	2				35.7	26.9	21.9
35	4	36	2				35.8	26.9	21.9
35	4	37	2				35.8	27.0	21.9
35	4	38	2				35.8	27.0	22.0
35	4	39	2				35.8	27.0	22.0
35	4	40	2				35.9	27.0	21.9
35	4	41	2				35.9	27.0	21.9
35	4	42	2				35.9	27.0	22.0
35	4	43	2				35.9	27.1	21.9
35	4	44	2				35.9	27.1	22.0
35	4	45	2				35.9	27.1	21.9
35	4	46	2				35.9	27.1	22.0
35	4	47	2				35.9	27.1	22.0
35	4	48	2				36.0	27.1	22.0
35	4	49	2				36.0	27.2	22.1
35	4	50	2				35.8	26.8	21.9
35	4	51	2				35.2	26.4	22.1
35	4	52	2				35.6	26.3	22.0
35	4	53	2				35.7	26.4	22.1
35	4	54	2				35.9	26.5	22.0
35	4	55	2	0	0	0.12	35.9	26.5	22.1
36	4	0	0	0	0	0.63	32.2	27.1	20.5
36	4	1	0				32.4	26.9	20.5
36	4	2	0				32.5	26.9	20.6
36	4	3	0				32.7	27.0	21.1
36	4	4	0				32.7	27.1	20.9
36	4	5	0				32.8	27.1	20.7
36	4	6	1				32.8	27.1	20.5
36	4	7	1				32.9	27.2	20.5
36	4	8	1				32.9	27.3	20.7
36	4	9	1				32.9	27.3	20.6
36	4	10	1				32.9	27.4	20.6
36	4	11	1				33.0	27.4	20.7
36	4	12	1				33.0	27.4	20.6

Table C 46. Continued

36	4	13	1				33.0	27.4	21.4
36	4	14	1				33.1	27.5	21.0
36	4	15	1				33.1	27.5	20.9
36	4	16	1				33.0	27.4	20.4
36	4	17	1				33.0	27.4	20.7
36	4	18	1				33.1	27.5	20.4
36	4	19	1				33.1	27.5	21.1
36	4	20	1				33.1	27.5	20.8
36	4	21	1				33.1	27.4	20.5
36	4	22	1				33.1	27.3	20.8
36	4	23	1				33.2	27.2	20.4
36	4	24	1				33.2	27.1	20.7
36	4	25	1	0	0	0.64	33.2	27.0	20.5
36	4	26	2				33.1	27.2	20.5
36	4	27	2				33.2	27.2	20.6
36	4	28	2				33.2	27.3	20.9
36	4	29	2				33.3	27.3	21.1
36	4	30	2				33.2	27.4	20.9
36	4	31	2				33.3	27.5	20.4
36	4	32	2				33.3	27.6	20.7
36	4	33	2				33.3	27.5	20.6
36	4	34	2				33.3	27.7	20.8
36	4	35	2				33.3	27.7	20.9
36	4	36	2				33.3	27.7	20.7
36	4	37	2				33.2	27.7	20.1
36	4	38	2				33.2	27.7	20.7
36	4	39	2				33.2	27.8	20.5
36	4	40	2				33.2	27.9	20.5
36	4	41	2				33.2	27.7	20.7
36	4	42	2				33.2	27.7	20.5
36	4	43	2				33.2	27.7	20.5
36	4	44	2				33.3	27.7	21.2
36	4	45	2				33.2	27.6	20.6
36	4	46	2				33.3	27.8	20.5
36	4	47	2				33.3	27.8	20.7
36	4	48	2				33.3	27.7	21.4
36	4	49	2				33.2	27.7	20.5
36	4	50	2				33.2	27.7	20.5
36	4	51	2				33.3	27.7	21.2
36	4	52	2				33.2	27.6	20.6
36	4	53	2				33.3	27.8	20.5
36	4	54	2				33.3	27.8	20.7
36	4	55	2	0	0	0.63	33.3	27.7	21.4
37	3	0	0	0	0	0.26	33.9	29.9	20.9
37	3	1	0				34.0	29.9	21.0
37	3	2	0				34.0	29.9	20.7
37	3	3	0				34.1	29.9	20.9

Table C 46. Continued

37	3	4	0				34.2	30.0	20.9
37	3	5	0				34.2	30.1	21.0
37	3	6	1				34.2	30.2	20.9
37	3	7	1				34.2	30.4	20.7
37	3	8	1				34.2	30.2	20.8
37	3	9	1				33.7	27.9	21.1
37	3	10	1				32.6	28.7	20.8
37	3	11	1				32.4	28.8	20.9
37	3	12	1				32.5	28.9	20.7
37	3	13	1				32.5	28.9	20.7
37	3	14	1				32.6	29.0	21.2
37	3	15	1				32.7	29.1	20.7
37	3	16	1				32.8	29.1	20.7
37	3	17	1				32.8	29.2	20.9
37	3	18	1				32.9	29.1	21.1
37	3	19	1				32.9	29.1	21.0
37	3	20	1				32.9	29.1	21.0
37	3	21	1				32.9	29.1	20.8
37	3	22	1				32.9	29.1	21.0
37	3	23	1				32.9	29.1	20.8
37	3	24	1				32.9	29.1	20.6
37	3	25	1	12	60	0.22	32.9	29.2	20.6
37	3	26	2				33.0	29.2	20.7
37	3	27	2				33.0	29.2	21.0
37	3	28	2				32.4	29.0	20.6
37	3	29	2				32.2	28.8	20.5
37	3	30	2				32.2	28.8	20.8
37	3	31	2				32.3	28.8	20.7
37	3	32	2				32.3	29.0	20.6
37	3	33	2				32.3	28.9	20.8
37	3	34	2				32.4	28.9	20.9
37	3	35	2				32.4	28.8	20.9
37	3	36	2				32.4	28.7	20.6
37	3	37	2				32.5	28.9	20.8
37	3	38	2				32.5	28.9	20.4
37	3	39	2				32.5	28.9	20.6
37	3	40	2				32.6	28.8	20.8
37	3	41	2				32.6	28.9	20.6
37	3	42	2				32.6	29.0	21.0
37	3	43	2				32.7	29.0	20.6
37	3	44	2				32.7	29.0	20.8
37	3	45	2				32.7	29.0	20.7
37	3	46	2				32.7	29.1	21.0
37	3	47	2				32.8	29.0	21.3
37	3	48	2				32.8	29.1	20.7
37	3	49	2				32.8	29.1	20.4
37	3	50	2				32.9	29.1	20.7

Table C 46. Continued

37	3	51	2				32.9	29.2	20.8
37	3	52	2				32.9	29.3	20.6
37	3	53	2				32.9	29.2	20.5
37	3	54	2				33.0	29.3	20.8
37	3	55	2	2	17	0.24	33.0	29.3	20.3
38	4	0	0	0	0	0.32	31.3	26.4	21.3
38	4	1	0				31.7	27.1	21.1
38	4	2	0				31.9	27.2	20.9
38	4	3	0				32.1	27.3	21.1
38	4	4	0				32.3	27.3	20.9
38	4	5	0				32.4	27.5	20.2
38	4	6	1				32.5	27.5	20.6
38	4	7	1				32.5	27.5	20.4
38	4	8	1				32.6	27.6	20.4
38	4	9	1				32.6	27.7	20.5
38	4	10	1				32.6	27.7	20.5
38	4	11	1				32.7	27.8	20.6
38	4	12	1				32.8	27.8	20.5
38	4	13	1				32.9	27.8	20.3
38	4	14	1				33.0	27.8	20.6
38	4	15	1				33.0	27.8	20.6
38	4	16	1				33.1	27.7	20.7
38	4	17	1				33.2	27.8	20.7
38	4	18	1				33.2	27.9	20.8
38	4	19	1				33.3	28.0	20.5
38	4	20	1				33.3	27.8	20.4
38	4	21	1				33.3	27.9	20.7
38	4	22	1				33.4	27.9	20.6
38	4	23	1				33.4	27.9	20.6
38	4	24	1				33.4	27.9	20.5
38	4	25	1	0	0	0.33	33.4	27.7	20.6
38	4	26	2				33.5	27.9	20.0
38	4	27	2				33.5	27.8	20.2
38	4	28	2				33.5	27.9	20.4
38	4	29	2				33.5	27.8	20.3
38	4	30	2				33.5	27.8	20.4
38	4	31	2				33.5	27.8	20.4
38	4	32	2				33.5	27.8	20.5
38	4	33	2				33.5	27.8	20.2
38	4	34	2				33.5	27.7	20.2
38	4	35	2				33.4	27.6	21.2
38	4	36	2				33.3	27.7	20.6
38	4	37	2				33.3	27.6	20.8
38	4	38	2				33.3	27.7	20.8
38	4	39	2				33.2	27.6	20.4
38	4	40	2				33.2	27.7	20.4
38	4	41	2				33.2	27.6	20.4

Table C 46. Continued

38	4	42	2				33.2	27.7	20.5
38	4	43	2				33.1	27.7	20.6
38	4	44	2				33.1	27.7	20.7
38	4	45	2				33.1	27.6	20.9
38	4	46	2				33.1	27.7	20.7
38	4	47	2				33.1	27.7	20.9
38	4	48	2				33.1	27.7	20.5
38	4	49	2				33.1	27.6	20.7
38	4	50	2				33.1	27.6	20.9
38	4	51	2				33.1	27.6	20.8
38	4	52	2				33.1	27.6	20.5
38	4	53	2				33.1	27.6	20.6
38	4	54	2				33.1	27.6	20.7
38	4	55	2	0	0	0.34	33.1	27.6	20.5
39	1	0	0	0	0	0.38	32.7	28.1	21.0
39	1	1	0				32.9	28.1	20.7
39	1	2	0				32.9	28.2	21.2
39	1	3	0				33.0	28.3	21.3
39	1	4	0				33.1	28.2	21.3
39	1	5	0				33.1	28.3	20.8
39	1	6	1				33.2	28.3	20.8
39	1	7	1				33.2	28.7	21.4
39	1	8	1				33.3	28.4	20.8
39	1	9	1				33.3	28.2	21.3
39	1	10	1				33.4	28.3	21.0
39	1	11	1				33.4	28.2	21.1
39	1	12	1				33.4	28.2	21.2
39	1	13	1				33.5	28.2	21.3
39	1	14	1				33.5	28.2	21.4
39	1	15	1				33.5	28.2	21.4
39	1	16	1				33.6	28.4	21.2
39	1	17	1				33.6	28.3	21.1
39	1	18	1				33.6	28.3	20.9
39	1	19	1				33.7	28.4	20.9
39	1	20	1				33.7	28.3	20.9
39	1	21	1				33.7	28.3	21.1
39	1	22	1				33.7	28.3	21.0
39	1	23	1				33.8	28.3	21.3
39	1	24	1				33.8	28.2	21.4
39	1	25	1	22	73	0.15	33.8	28.2	20.9
39	1	26	2				33.8	28.2	21.0
39	1	27	2				33.8	28.2	21.0
39	1	28	2				33.8	28.2	21.1
39	1	29	2				33.6	28.1	21.6
39	1	30	2				33.4	28.1	21.1
39	1	31	2				33.3	28.0	21.1
39	1	32	2				33.2	28.0	21.4

Table C 46. Continued

39	1	33	2				33.2	27.9	21.2
39	1	34	2				33.2	27.9	20.9
39	1	35	2				33.2	27.9	21.4
39	1	36	2				33.2	27.9	21.3
39	1	37	2				33.2	27.9	21.5
39	1	38	2				33.2	27.9	20.8
39	1	39	2				33.2	28.0	21.1
39	1	40	2				33.2	28.0	20.4
39	1	41	2				33.2	28.0	20.9
39	1	42	2				33.2	27.9	20.8
39	1	43	2				33.2	28.1	21.2
39	1	44	2				33.2	28.2	20.7
39	1	45	2				33.3	28.1	20.9
39	1	46	2				33.3	28.2	21.1
39	1	47	2				33.3	28.2	20.6
39	1	48	2				33.3	28.2	21.0
39	1	49	2				33.3	28.2	20.8
39	1	50	2				33.3	28.3	20.6
39	1	51	2				33.3	28.3	20.7
39	1	52	2				33.3	28.3	20.9
39	1	53	2				33.3	28.4	20.8
39	1	54	2				33.3	28.1	21.2
39	1	55	2	4	11	0.29	33.3	28.4	21.1
40	3	0	0	0	0	0.28	34.0	27.1	20.6
40	3	1	0				33.2	26.8	20.8
40	3	2	0				31.9	26.3	20.8
40	3	3	0				31.8	26.3	20.8
40	3	4	0				31.9	26.3	20.5
40	3	5	0				32.0	26.3	20.6
40	3	6	1				32.2	26.2	20.7
40	3	7	1				32.3	26.2	20.6
40	3	8	1				32.5	26.2	20.6
40	3	9	1				32.6	26.2	20.6
40	3	10	1				32.7	26.3	20.8
40	3	11	1				32.8	26.2	20.9
40	3	12	1				32.9	26.3	20.9
40	3	13	1				32.9	26.3	20.9
40	3	14	1				33.0	26.3	20.7
40	3	15	1				33.0	26.3	20.4
40	3	16	1				33.1	26.3	20.9
40	3	17	1				33.1	26.4	20.7
40	3	18	1				33.1	26.4	20.2
40	3	19	1				32.2	25.9	20.8
40	3	20	1				32.1	25.8	21.0
40	3	21	1				32.1	25.8	21.0
40	3	22	1				32.1	25.8	20.8
40	3	23	1				32.2	25.8	20.5

Table C 46. Continued

40	3	24	1				32.3	25.9	21.0
40	3	25	1	6	16	0.15	32.4	25.9	21.3
40	3	26	2				32.5	25.9	21.1
40	3	27	2				32.5	26.0	21.4
40	3	28	2				32.6	25.9	20.9
40	3	29	2				32.7	26.0	20.7
40	3	30	2				32.8	26.0	20.9
40	3	31	2				32.9	26.0	20.9
40	3	32	2				32.9	26.1	20.4
40	3	33	2				33.0	26.1	20.8
40	3	34	2				33.0	26.1	20.7
40	3	35	2				33.1	26.1	20.7
40	3	36	2				33.1	26.1	20.7
40	3	37	2				33.1	26.1	20.4
40	3	38	2				33.1	26.1	20.3
40	3	39	2				33.1	26.1	20.9
40	3	40	2				33.2	26.2	20.6
40	3	41	2				33.2	26.1	20.6
40	3	42	2				33.2	26.1	20.5
40	3	43	2				33.2	26.2	20.7
40	3	44	2				33.2	26.2	20.6
40	3	45	2				33.2	26.1	20.9
40	3	46	2				33.2	26.2	20.8
40	3	47	2				33.3	26.1	20.6
40	3	48	2				33.7	26.4	20.4
40	3	49	2				34.1	26.4	20.7
40	3	50	2				34.2	26.3	20.7
40	3	51	2				34.3	26.4	20.8
40	3	52	2				34.2	26.3	20.6
40	3	53	2				34.2	26.3	20.7
40	3	54	2				34.1	26.3	20.6
40	3	55	2	4	6	0.15	34.1	26.2	20.6

Sub = subjects
Cond = condition
PRI = pain rating index
VAS = visual analogue scale
H:M = Quadriceps H:M_{max} ratio
Pat. = patella surface temperature
Pop. = popliteal surface temperature
Amb. = ambient temperature

Appendix D

Clinical Implications

Clinical Implications

The use of an experimental pain model may be useful in examining the effects of therapeutic modalities. From our observation a 20-minute cryotherapy treatment immediately decreased the experimentally induced anterior knee pain within the first minute of application with a gradual decline during and following application.

It is now apparent that pain in the absence of joint effusion is a contributing factor to arthrogenic muscle inhibition. When cryotherapy is applied to the anterior knee to reduce pain, it also facilitates motoneuron pool recruitment. Clinicians should consider incorporating a 20-minute cryotherapy treatment prior to therapeutic rehabilitation in help minimize pain (as measured with a visual analogue scale) and facilitate knee joint exercise.

Appendix E

Recommendations for Future Research

Recommendations for future research to extend the results of this dissertation

- Determine if pain caused by intermittent infusion of hypertonic saline alters voluntary motoneuron pool activation.
- Determine if various cryotherapy temperatures influence motoneuron pool activation.
- Determine if different pain intensities and cryotherapy influence motoneuron pool disinhibition and facilitation.
- Determine if the intermittent infusion of hypertonic saline with a sham ice bag increases pain perception more than infusion of saline without sham application.
- Determine if the intermittent infusion of hypertonic saline stimulates the release of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA).
- Determine if knee joint effusion or pain is the primary factor causing AMI.
- Determine if thermotherapy decreases perceived pain during intermittent infusion of hypertonic saline into the anterior knee.
- Determine if transcutaneous neuromuscular facilitation decreased perceived pain during intermittent infusion of hypertonic saline into the anterior knee.