ANXIETY, APPLIED TENSION, AND VASOVAGAL

SYMPTOMS IN BLOOD DONORS.

CRYSTAL D. HOLLY

B.Sc.

Department of Psychology

McGill University

Montreal, Québec, Canada

December 2011

A thesis submitted to McGill University in partial fulfillment of the requirements

of the degree of Doctor of Philosophy

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DEDICATION

To my family and friends.

ACKNOWLEDGEMENTS

I would like to express my gratitude for the many people who supported, encouraged and assisted me in the processes of achieving this goal. First, to my supervisor, Dr. Blaine Ditto who was patient and provided gentle guidance throughout the time it took me to complete my research and prepare my dissertation. His ability to let me follow my own path yet to nudge me back when I strayed too far was invaluable in getting me to this point.

I was fortunate to share my laboratory with excellent students, both graduate and undergraduate. Without my partner in research from the early days, Sarny Balegh, this process would have been much more arduous and challenging and certainly less fun. Your patience in listening to my problems and constant availability for sorting out a problem or just a simple chat will never be forgotten. Likewise, I graciously appreciate the countless hours of time spent in blood donation clinics, entering and processing data and smiles of Shazia Abji, Giselle Kraus, Lindsey Torbit, and Daniella Ladowski. My research in this laboratory was generously funded by Canadian Institutes of Health Research, Canadian Blood Services and the Fonds de Recherche en Santé du Québec.

To my fellow students, Laurel Patterson, Ilana Kronick, Julie Mercier and Seth Davis. I have been fortunate to be surrounded by such bright, inspiring and wonderful friends since day 1 in this program. You all have contributed so much to both my personal and professional development and your friendship and encouragement ensured that every single day of my Ph.D. was a good one.

From my earliest memories my family has supported me in all my decisions, wise or not, and have stood by me and encouraged me to be all I can.

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Thank you to my parents and siblings for supporting me in all ways throughout this thesis as I would not be here without you. Lastly, to Jean-Christophe, for pushing me to always be better but then for telling me that I'm already the best. You're my balance and you keep me on track with your unwavering belief in me.

CONTRIBUTION OF AUTHORS

As the first author on both of the manuscripts, I took the lead role in the research, design, implementation, analyses, interpretation and writing of all manuscripts. The first manuscript is co-authored by Sarny Balegh, a fellow graduate student who assisted in the collecting and analysis of data. The second manuscript is co-authored by Lindsey Torbit, a research assistant, who also assisted in the collecting and analysis of data. My supervisor, Dr. Blaine Ditto, third author on both manuscripts, provided substantial input into the design, analyses, and interpretation of the data. He also provided excellent editorial comments through preparation of the manuscripts.

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ABSTRACT

Vasovagal symptoms include feelings of dizziness, lightheadedness, nausea and may even culminate in vasovagal syncope, commonly known as a faint. There is a well-documented association between blood, injection and injury (BII) fears and experiencing vasovagal symptoms. Applied Tension (AT) is a behavioural technique that involves repeated tensing and releasing of upper- and lower-body muscles in 5-second intervals while maintaining steady, regular breathing. This repeated tensing prevents the rapid drop in blood pressure that occurs during vasovagal reactions. There is well documented literature supporting the effectiveness of this technique, however, the mechanisms through which it is works are not well understood. This research explored the relationship among vasovagal symptoms, BII fears and AT. The first aim was to explore if AT is effective in reducing vasovagal symptoms in part through anxiety reduction. The second aim built upon this idea and sought the optimal timing of AT in reducing vasovagal symptoms. In Manuscript One, a principally laboratory-based study with a supplementary review of clinical data, physiological measures were obtained while participants watched a video depicting blood draws. AT reduced vasovagal symptoms in higher fear females. This reduction in symptoms was due more to decreases in anxiety than exerciserelated cardiovascular change. In Manuscript Two, a randomized clinical trial, AT was applied prior-to, during, or both prior-to and during blood donation. AT was effective in reducing vasovagal symptoms in blood donors, particularly when practiced prior to donation. Donors that used AT prior to donation required less treatment in the blood donor clinic for vasovagal reactions than individuals who

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did not. Again, these results support the notion that the effects of AT are not only due to exercise-related cardiovascular change and that they may be through a reduction of anxiety. In sum, these findings suggest that AT is an effective treatment of vasovagal symptoms and syncope and that anxiety reduction plays an important role. Future research is recommended on the role of anxiety in the vasovagal response.

RÉSUMÉ

Les symptômes vasovagaux comprennent des sensations d'étourdissement, des nausées et peuvent même aboutir à une syncope vasovagale, connue sous le nom de perte de connaissance. Il existe une association bien documentée entre les craintes associées au sang, aux injections et aux blessures, et les symptômes vasovagaux. La tension musculaire appliquée (TMA) est une technique comportementale qui consiste à contracter certains muscles de façon répétitive par cycles de 5 secondes tout en maintenant une respiration régulière et constante. Ces contractions répétitives empêchent la chute rapide de la pression sanguine qui survient au cours des réactions vasovagaux. Il existe une littérature bien documentée montrant l'efficacité de cette technique, cependant les mécanismes aux travers desquels elle est efficace ne sont pas bien compris. Cette recherche à exploré la relation entre les symptômes vasovagaux les craintes associées au sang, aux injections et aux blessures, et la TMA. Le premier objectif de cette recherche est d'étudier si la technique de la TMA est efficace pour réduire les symptômes vasovagaux en partie due à la réduction de l'anxiété. Le deuxième objectif repose sur la théorie que la technique de la TMA est efficace grâce à la réduction de l'anxiété et explore quel el le timing optimal de TMA pour réduire les symptômes vasovagaux. Dans le « Manuscript One », consistant d'une étude mise en œuvre principalement en laboratoire et complémentée d'une recherche de données cliniques, des mesures physiologiques ont été obtenues alors que les participants regardaient une vidéo montrant une prise de sang. La TMA a réduit les symptômes vasovagaux chez les femmes aves des peurs médicales plus élevées. Cependant cette réduction des symptômes est davantage attribuable à une

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diminution de l'anxiété, plutôt qu'à des changements cardiovasculaires liés à l'exercice. Dans le « Manuscript Two », lors d'un essai clinique randomisé, la TMA a été appliquée avant, pendant, ou bien avant et pendant le don de sang. La technique de la TMA réduit efficacement les symptômes vasovagaux chez les donneurs de sang, en particulier lorsqu'elle a été pratiquée avant le don. Les donneurs qui avaient pratiqué la TMA avant le don de sang avaient besoin de moins de traitement dans la clinique pour les réactions vasovagaux que les donneurs de sang qui n'avaient.pas pratiqué la TMA. Encore une fois, ces résultats confirment la notion selon laquelle les effets de l'AT ne sont pas seulement dus à des changements cardiovasculaires liés à l'exercice, et que la réduction de l'anxiété joue un rôle. En somme, ces résultats suggèrent fortement que l'AT est un traitement efficace des symptômes et de la syncope vasovagale et que la réduction de l'anxiété joue un rôle. Des recherches futures sont recommandées sur le rôle de l'anxiété dans la réponse vasovagale.

GENERAL INTRODUCTION

Current Blood Supply

In Canada, approximately every minute someone needs a blood donation (Canadian Blood Services, 2011). In order to maintain a blood supply that meets the ever-increasing demands, there must be a strong donor base. Yet reality is far different. It has been estimated that only 3% of the Quebec population donates blood, consistent with reports from other developed countries with similar blood donations systems (e.g., Australia and the United States) (Davey, 2004; Godin et al., 2005). However, the rates of eligible donors are much higher. For example, in the United States, estimates indicate that between 1/3 to 2/3 of the adult population is eligible to donate blood depending on exclusion criteria (Reid & Wood, 2008; Riley, Schwei, & McCullough, 2007). Research is needed to determine why eligible donors do not give blood and to investigate possible ways to encourage this activity.

In addition to the small pool of current donors, the aging population will create further strain on the blood donation system. The need for blood could double in the near future as individuals over 65 years use more than 40% of the blood supply and new uses are developed for blood products (Zuck et al., 1995). In order to maintain the blood supply, an approximate 2% increase yearly in new donors is necessary. If the donor pool does not grow in Canada, demand could outpace the supply as early as 2012 (Drackley, Newbold, Paez, & Heddle, 2011). At the same time, as tools to diagnose communicable and blood borne diseases increase, the donor pool decreases due to restrictions placed upon potential donors, also known as deferrals (Linden, Gregorio, & Kalish, 1988). This has

already compounded the issue. Canada maintains strict rules on potential blood donors' eligibility, screening and eliminating donors for a number of reasons.

In any voluntary blood system, donors are typically deferred for one of four reasons: self-reported exposures, medical evaluation, previous screening results, or historical deferral found in blood center databases (Custer et al., 2004). Though ability to screen blood for transmissible disease has increased significantly, the most practical procedure is to defer prospective donors according to risk or reports of exposure to a pathogen based on travel history and behaviour. Historically, strict screening began with the recognition of acquired immunodeficiency syndrome (AIDS) in the 1970's and early belief that it was due to an undetectable virus (now known to be the human immunodeficiency virus or HIV) (McCullough, 1993). In the early 1980's the first cases of individuals who contracted AIDS through blood transfusion emerged. Transfusion of contaminated blood opened the door for massive lawsuits and was bankrupting blood collection organizations. This crisis led to the development of sometimes controversial screening based on statistical risk factors (McCullough, 1993) to ensure a safe supply for blood recipients. This testing system is constantly in evolution to ensure that with the development or discovery of emerging pathogens (e.g., variant Creutzfeldt-Jakob disease) new criteria are added to the screening. Thus, the system is usually believed safe due to the combination of eligibility screening and post-collection blood testing; however, it results in a high donor refusal rate.

Riley and colleagues (2007) estimate that only 37.8% of the United States population would be eligible to donate blood if all exclusion criteria are

considered. In sum, while other factors are involved, the blood system is stretched due to high and increasing demand, high and increasing restrictions on who can give blood, and a somewhat general state of public apathy about the problem. The idea of public apathy is supported not only by the relatively small percentage of the population that gives blood but the large increases that have been observed following natural (Busch et al., 1991; Wiwanitkit, 2005) and manmade disaster (Glynn et al., 2003; Sullivan, Cotten, Read, & Wallace, 2007).

A related and perhaps even more alarming problem is that the retention rates of actual donors is low and has been dropping in recent years. That is, people who were eligible and enthusiastic enough about the idea of blood donation to try it once often do not return. Canadian Blood Services states that of new Canadian donors, only 50% are estimated to return to be repeat donors (2009). This problem extends beyond North America. In a recent report, the United Kingdom's National Health Service (NHS) reported a decrease in young donors (between the ages of 17 and 34 years old) (National Health Services Blood and Transfusion Unit, 2011). This survey of 1,700 non-donors and 1,000 donors found that only 4% of current blood donors are under 30 years of age and most are above 40. They currently have 60,000 fewer young donors than 10 years ago (National Health Services Blood and Transplant Unit, 2011). As the blood supply is entirely dependent on donors this evidence demonstrates that blood supplies are facing a unique and serious problem.

Why People Do and Do Not Give Blood

To understand why there is such a struggle with the limited blood supply, it is important to understand motives and barriers to blood donation. Initially,

theory and research in the field suggested that altruism was the main reason that people give blood. That is, altruism in the sense that there is no direct benefit for the blood donor, only the recipient (Gillespie & Hillyer, 2002; Sojka & Sojka, 2008). While most people self-report that general altruism is the main reason they give blood, followed by social obligation and social influence (Sojka & Sojka, 2008), this may not be the entire story. More recent research on motivation to give blood indicates that "benevolence" is involved as well as altruism (Ferguson, France, Abraham, Ditto, & Sheeran, 2007; Gillespie & Hillyer, 2002; Sojka & Sojka, 2008). Ferguson and colleagues (2007) believe "altruism" to be a potential misnomer in most cases. Whereas an altruistic act is one without benefit to the donor and solely benefits others without external reward, blood donation appears to also include a personal reward to the donor in the form of the satisfaction of performing a helping behaviour. This view is supported by reports of positive social reinforcement and increased mood after donation (Ferguson et al., 2007) and perhaps even a sense of moral superiority in some cases (Masser, White, Hyde, & Terry, 2008). Of course, this does not diminish appreciation of this activity or imply it is "selfish". The benefits to society far outweigh these subtle rewards. However, viewing it as primarily a benevolent act that provides at least some benefit to the donor clarifies the situation and may provide clues for recruitment and interaction. For example, a recent public advertising campaign in the U.K. encouraged people to "do something amazing". Other documented motivators for blood donation include tangible incentives inherent in the procedure such as ensured blood replacement and blood credits (in some

jurisdictions), items of small value, post-donation food, and especially a free medical check-up (Gillespie & Hillyer, 2002).

Nevertheless, despite growing understanding of the positive motivations for blood donation, the rates remain low. This has led to research on the complementary question of why more individuals do not donate blood. For some, the issue appears to be simple lack of knowledge. Many potential donors state that they are not aware of the need for blood donation (Gillespie & Hillyer, 2002; Sojka & Sojka, 2008) or believe, incorrectly, that they are ineligible to give blood (Germain, Decary, Chiavetta, & Goldman, 2000; Gillespie & Hillyer, 2002). In some cases, news of blood donation requirements, exclusion criteria, and risks become muddled. Indeed, a small number of people believe that blood donation may involve risk to them of contracting disease. Others acknowledge the problem in principle but state that they are too lazy or not that impressed by the seriousness of the issue (Sojka & Sojka, 2008).

The notion that giving blood is inconvenient is also well-documented as a barrier to donation (Schreiber et al., 2006). Even if they believe it important, many perceive the donation process as lengthy (time constraints) and that clinics are not easily accessible (physical constraints). It is also important to consider those that have donated once, yet choose to not return for any subsequent donations. Along with the previously stated reasons, these individuals also often cite issues that occurred during the blood donation process. These range from a generally bad experience to problems with staff or treatment during the donation process. In particular, as will be discussed further later, unpleasant vasovagal symptoms is one of the most frequent explanations given for not returning to

donate (Schreiber et al., 2006). A similar and common explanation cited both by people who have never given blood and those who have tried it before is fear of the process (Gillespie & Hillyer, 2002; Schreiber et al., 2006; Sojka & Sojka, 2008). Indeed, though as previously discussed there are many possible reasons not to give blood, this may be the main reason, with other explanations offered as an "excuse" for this sensitive topic.

Fears and Blood Donation.

In a NHS survey, 37% of non-donors reported having fears associated with the blood donation process (National Health Service Blood and Transplant Unit, 2011). Frequently reported fears include usually related fears of fainting, needles and blood (Moore, 1991; Sojka & Sojka, 2008). Given the volunteer nature of the system, people with serious fears of needles or blood, or even mild ambivalence, can and do avoid giving blood. Some studies have revealed that fears are the primary source for avoidance of participating in blood donations for one quarter to one third of non-donors (Gillespie & Hillyer, 2002) and this figure may be higher. This fear is complex. While some individuals have an outright fear of blood, needles, or injections, occurring in upwards of 1/6 to 1/4 of non-donors (Gillespie & Hillyer, 2002), others state that their reason for non-donation is a perception that fear and pain may be associated with needles and the blood donation process (Reid & Wood, 2008); that is, they are more afraid of situational factors and thoughts of what may happen than the actual needles themselves.

In addition to this "fear of fear" and fear of pain, there may be concern that fear-related vasovagal symptoms such as dizziness and fainting may be uncomfortable, and possibly embarrassing. In investigating intentions of blood

donors, Reid and Wood (2008) differentiated between fear of needles and fear of the process also termed lack of control. They found that while highly correlated, these two fears constitute separate domains.

While it may seem that fear occurs only in people who have never given blood before, similar processes have been observed in people who have tried giving blood. This includes a large group of individuals who once had the intention to give blood regularly yet did not return after the initial donation. Schreiber (2003) estimated that only 33 percent of first-time donors give again within 1 year and that 50 percent do not return to donate within 5 years. In a recent survey of blood donors, Sojka and Sojka (2008) reported that 15% of donors state "fear of needles", "fear of fainting", and/or "fear of looking at blood" as the primary obstacle to overcome in order to become a regular blood donor. Similarly, Ditto and France (Ditto & France, 2006) found that women who experienced anxiety before giving blood were less likely to return in the following year to donate again. It is useful to note that, while these fears are exaggerated in some cases, they are not entirely baseless. Blood donation involves venipuncture with a large needle (typically 16 gauge) and extraction of a non-trivial quantity of blood, usually 450 mL (throughout North America and Europe) which represents approximately 1/10th of the total blood volume. Depending on the phlebotomist's skill, insertion of the needle may involve significant pain and can produce bruising after the donation. Further, while blood volume is rapidly replenished, even in the elderly (total volume occurs in 48-72 hours and the red cell replacement, while slower, is nonetheless completed in 3-6 weeks (Klein &

Anstee, 2007), even uneventful blood draws can lead to dizziness and weakness without being compounded by a vasovagal reaction.

Blood and Needle Fears in the General Population

These blood and needle fears reported in blood donation settings are also very common in the general population. Prevalence estimates of blood, injection and injury (BII) phobia, the severe end of the spectrum, range from 3.1% to 4.9% of the population (Vögele, Coles, Wardle, & Steptoe, 2003) and more commonplace fears of blood and needles are much higher, occurring in up to 20% of the general population(Wright, Yelland, Heathcote, Ng, & Wright, 2009). Indeed, few can be described as having no fear. BII phobic individuals experience intense, irrational, and persistent fear when they confront or anticipate exposure to injuries, blood, and wounds, which often leads to avoidance of medical procedures (Kleinknecht & Lenz, 1989). The pattern of avoidance of medical situations undoubtedly decreases the available number of blood donors and subsequent blood donations, thus further aggravating the blood supply problem as suggested by the low rates of actual donors and high rates of single donation donors. More concerning though are not the phobic individuals, but those with milder fears who nonetheless avoid the blood donation clinic because of a discomfort or unease.

The Vasovagal Response: Overview

In addition to the prevalence of fears of needles and blood, which may have evolutionary implications (Diehl, 2005) an unusual feature is the pattern of physiological activity that is different than those of other fears. While most fears and phobias result in a typical anxiety-provoked "fight or flight" response,

individuals with blood and injection fears tend to react very differently. The typical response in most fearful situations includes sympathetic activity leading to increases in heart rate, blood pressure, and respiration to support physical activity that may involve fighting or attempting to flee the feared stimuli. However, the opposite may occur in the face of blood, injections and injury. There is an atypical response, discussed in more detail later, which includes reduced heart rate and blood pressure (Engel, 1978), possibly culminating in feeling dizzy or experiencing a full faint. This pattern is known as a vasovagal response and the faint as vasovagal syncope. When investigating the differences between other fears or phobias and blood donation fears the question arises of why only with the latter do fainting like-reactions occur?

Systematic research on this set of symptoms began during the Second World War. As medical technology advanced, blood donation became commonplace and necessary to support soldiers at war. Although initially anecdotal, researchers began recording common side effects associated with donation. Vulnerable or at risk donors were noted to be young, female, novice donors, those with a history of fainting, and those that were considered "asthenic habitus" (slender build with long limbs or with a weak body or without strength) (Brown & McCormack, 1942; Greenbury, 1942; Poles & Boycott, 1942; Taylor, 1942; Williams, 1942). These at risk or vulnerable donors described experiencing nausea, illness and even fainting during donation. In 1961, Graham attempted to define prospectively factors associated with difficulties during blood donation. His research findings endorsed the previously suggested factors (i.e., young, female) and in addition he found that donors who reported increased nervousness

or anxiety tended to experience more reactions (Graham, 1961). Described as "psychogenic factors", this was the first time that emotional status was documented as playing a role in blood donation reactions.

The Vasovagal Response: Physiological Issues.

While research investigating vasovagal syncope and blood donation began in the mid 1900's, vasovagal syncope was studied for some time before this. The phrase "vasovagal" was first used early 1900s to describe the physiological precursor to most cases of fainting (Growers, 1907). A number of investigators (e.g., Wolf, 1958) speculated that there may be a progression from an aroused to a non-aroused state when this occurred. Graham, Kabler, and Lunsford (1961) formalized the idea by describing the vasovagal reaction as a "diphasic" response. They also viewed it as a somewhat paradoxical response. They believed an abrupt deceleration in heart rate and increase in vasodilation was usually preceded by a period of heart rate acceleration and vasoconstriction. The paradoxical component was the presumed large drop in blood pressure and heart rate. These blood pressure and heart rate increases and decreases were thought to be the result of mixed patterns of sympathetic nervous system (SNS) and parasympathetic nervous system (PNS) activity. It is now well-established that SNS and PNS stimulation of the heart is not necessarily always complementary (e.g., increased SNS activity associated with decreased PNS activity). Both branches of the autonomic nervous system may stimulate the heart at the same time (Berntson, Norman, Hawkley, & Cacioppo, 2008).

Historically, the first part of the vasovagal response is viewed as a typical fear-oriented reaction associated with SNS activity that leads to increases in HR

and BP (Page, 1994). Presumably, this is followed by a fast and dramatic decrease in SNS activity and an increase in PNS activity that leads to decreases in HR and BP, to the extent that cerebral perfusion may diminish creating symptoms of dizziness, weakness, and possibly syncope (Vögele et al., 2003). The phrase "vasovagal" reaction was coined in 1932 by Lewis and reflects the thinking that symptoms spring from decreased blood pressure due to a combination of sympathetic withdrawal leading to vasodilation and parasympathetic activity leading to vagal stimulation and heart rate deceleration.

While a useful point of reference, this term may be unfortunate for several reasons especially the presumption of a key role for vagal stimulation. For example, it has been known for many years that pre-treatment with the cholinergic blocker atropine does not prevent vasovagal reactions (Lewis, 1932). The role of vasodilation has also been emphasized increasingly, leading many to prefer the term "vasodepressor response". Another issue is the relevance, if any, of peripheral changes in heart rate and blood pressure. For example, as will be discussed later, Ritz et. al. (2010) have recently proposed that the most important inhibitory effects come from hyperventilation-induced hypocapnia that produces cerebral vasoconstriction and hypoxia.

One issue that has always puzzled researchers who focus on changes in heart rate and blood pressure is the mechanism for the assumed switch from an excitatory to inhibitory state. Although a number of ideas have been proposed, the most widely accepted view for many years focussed on the activity of cardiac stretch receptors. In principle, like all baroreceptors, they function as part of a negative feedback loop. Decreased cardiac filling elicits increases in SNS activity

and decreases in PNS activity in an attempt to stabilize blood pressure through vasoconstriction and heart rate acceleration. The reverse normally happens with increased cardiac filling. However, using a model developed using animals exposed to extreme haemorrhage, it was proposed that reductions in cardiac filling may occasionally elicit maladaptive vasodilation and heart rate deceleration if the heart contracts around a nearly empty chamber, accidentally stretching these receptors (van Lieshout, Wieling, Karemaker, & Eckberg, 1991). This might be able to explain the second phase of the vasovagal reaction as a decrease in filling could be caused by blood loss, postural change (going to an upright posture), psychological stress or the combination of these variables as often occurs during blood donation.

In recent years, this theory has been challenged by several different kinds of observations such as the fact that vasovagal reactions can be observed in deafferented heart transplant recipients (Mosqueda-Garcia, Furlan, Tank, & Fernandez-Violante, 2000). It remains an important concept though other developments may ultimately make the model less relevant to emotional fainting. For example, in addition to questioning the importance of peripheral changes in hear rate and blood pressure, Ritz and colleagues (2010) have also questioned whether or not the vasovagal response is truly diphasic. Stress-related decreases in physiological activity are an intrinsic part of the response but it is not clear if these are always preceded by a more aroused state. Hence, the idea of a transition mechanism from excitatory to inhibitory state may be unnecessary.

The Vasovagal Response: Psychological Components.

Syncope is a transient loss of consciousness not due to head trauma (e.g., concussion), drug use, epilepsy, etc. (Thijs, Wieling, Kaufmann, & van Dijk, 2004). In turn, syncope can be due to a variety of cardiovascular problems such as arrhythmias and neural control of cardiovascular activity. Vasovagal syncope is the most common cause of loss of consciousness (Sheldon et al., 2005). It is often due to emotional stress though a variety of physical stressors such as blood loss, heat, and postural change, also elicit vasovagal reactions. Individuals with syncope report significant levels of psychological distress and even psychiatric comorbidity (e.g., anxiety) (D'Antono, Dupuis, St-Jean, Lévesque, Nadeau, Guerra, et. al., 2009). One reason in support of the diphasic concept is that all of these stimuli are capable of producing increases in SNS activity. Syncope occurs quite frequently in the general population. In the Framingham Study, 10.5% of the population reported at least one episode of syncope over a 17-year period (Soteriades et al., 2002). Higher rates than this have been noted in some more specialized and closely monitored populations. For example, several studies of military groups found lifetime rates from 20 - 27% (Dermkasian & Lamb, 1958; Lamb, Green, & Combs, 1960; Murdoch, 1980). Much more rare, but nonetheless relevant, are occasional examples of syncope followed by sudden death subsequent to a psychological stressor. Although these cases typically involve some pre-existing cardiac vulnerability, what is striking is the onset of the condition following a highly emotional situation (Engel, 1978).

Another example of a healthy group that reports high levels of fainting is medical students. One study found that 39% of a group of first to fourth year medical students reported at least one lifetime incident of syncope (Ganzeboom,

Colman, Reitsma, Shen, & Wieling, 2003). While their figures reflect lifetime values (and hence include childhood experiences) and many of the participants noted multiple triggers such as prolonged standing and being in a warm room, 39% of those who experienced syncope said that some combination of observation of pain, emotion, venipuncture, and blood was involved.

The most common contexts for fainting and pre-faint symptoms seem to be those that involve medical, dental, and injury related situations; in essence it appears that fainting most commonly occurs in contexts involving blood, needles or injections (Öst, Sterner, & Lindahl, 1984; Page, 1994). While fainting rarely occurs in the context of other feared stimuli (less than 1%), it is commonplace and ranges between 5 and 15% when blood is involved (Canadian Blood Services, 2010; Page, 1994). Engel (1978) proposed two conditions that together increase the probability of vasovagal syncope: firstly, the threat of an unfamiliar or difficult to cope with physical injury, and secondly when the individual is expected to face this situation with calm or courage. This description closely matches what some individuals might feel in the blood donation context, particularly first time donors.

In their research investigating cardiovascular reactions to feared stimuli, Öst and colleagues (1984) found physiological evidence supporting Graham's theory of a biphasic reaction. In a laboratory evaluation of blood phobics observing thoracic surgery, they monitored HR and BP and observed that participants displayed a diphasic response while viewing the film. However, participants were able to turn off the film and the vasovagal response dissipated when they did so, showing the relation of the vasovagal reaction to the feared

stimuli. Further support for the involvement of emotion in vasovagal syncope, particularly in the context of needles, stems from the timing of the episode of syncope. The majority of cases of vasovagal syncope during venipuncture occur after the needle has been removed from the arm suggesting that there is not due to a medical issue though at this point all the blood that is going to be withdrawn, has (Ruetz, Johnson, Callahan, Meade, & Smith, 1967). This is consistent with one of the psychological theories of vasovagal syncope noted before, i.e., Graham's (Graham et al., 1961).

Engel proposed two models that were somewhat similar and emphasized simultaneous excitatory and inhibitory processes. In general, he suggests there is a conflict between Cannon's sympathetically mediated fight/flight response, as a preparation for action, and a conservation/withdrawal reaction (parasympathetically mediated). This second response of conservation and withdrawal may also be an attempt to find safety through a loss of awareness/consciousness in the face of danger. It involves disengagement, withdrawal, and inactivity in the efforts to conserve energy and to disengage with a hostile environment. In turn, this may make the organism less noticeable to predators. Engel believed that this conflict may lead to sustained or alternating activation of the two emergency systems. In his thinking, this explained several observations such as continued large muscle vasodilation in the face of muscle inhibition.

In contrast, Graham's model (1961) proposed that the faint occurs due to the sudden removal of anxiety. Homeostatic antagonistic responses that presumably had been elicited to offset strong sympathetic responses and

cardiovascular activation (e.g., baroreceptor mediated PNS activity) were then left unopposed with the cessation of the stressor resulting in the sudden faint. Other more recent perspectives focus more explicitly on the possible adaptive value of vasovagal syncope. For example, Bracha has argued that prehistoric people who fainted when faced with overwhelming opponents were more likely to survive the encounters (Bracha, 2004; Bracha, Bracha, Williams, Ralston, & Matsukawa, 2005).

A similar but more nuanced idea was presented by Diehl (2005) who suggested that emotion-related fainting is based in the more fundamental process of hemorrhagic fainting. Fainting in response to significant blood loss of approximately 30% total volume appears to be nearly universal across species. Diehl argues that this cannot be explained by blood loss per se. Rather, it is an adaptive reflex to reduce metabolism, blood pressure, and as a result, blood loss. He suggests that psychologically related fainting may have originated as anticipation or belief of significant blood loss. In a recent study of blood donors who had an identical amount of blood withdrawn, Ditto et. al. (Ditto, Balegh, Gilchrist, & Holly, 2011) found that subjective ratings of perceived blood loss were significantly associated with vasovagal symptoms independent of anxiety. The anticipation or belief of blood loss triggered vasovagal symptoms similar to those that may occur during an actual haemorrhage. This may provide an explanation for the interesting finding noted before; that many needle-related reactions occur after removal of the needle. At this point, there may still be a belief or feeling of blood loss. An additional advantage of this perspective is that

the physiological mechanisms of hemorrhagic fainting are fairly well described (Diehl, 2005).

Disgust is another potential psychological contributor that has been discussed in relation to blood and needle fear, and fainting (Page, 1994). Disgust is typically described as a basic emotion involving revulsion at the prospect of oral consumption of an offensive object (Rozin & Fallon, 1987). This serves as a protective mechanism against ingestion of poisonous or otherwise noxious substances. However, ingestion is not necessary to elicit disgust and feelings are often caused by the sight of needles or blood. Disgust closely mirrors vasovagal syncope both in the physiological response patterns as well as symptoms elicited with the experience (e.g., nausea and vomiting). Conversely, these similarities are not also shared by fear. To further support the link between disgust and syncope, research shows that individuals more fearful of blood and injury are more likely to report feelings of disgust (Page, 1994, 2003; Sawchuk, Lohr, Tolin, Lee, & Kleinknecht, 2000) and those that faint are also more sensitive to disgust (Page, 2003).

Page (1994) describes vasovagal syncope as the result of a "dual process" in which an arousing, fearful state is followed or accompanied by a growing sense of disgust over the possibility of a body envelope violation. This theory fits well that of the blood donation situation, in which several body envelope violations would occur (e.g., finger prick, needle insertion). However, some research has shown that disgust does not contribute to fainting in response to blood stimuli after fear is accounted for (Kleinknecht, Thorndike, & Walls, 1996; Olatunji, Williams, Sawchuk, & Lohr, 2006). In sum, while psychological factors are

clearly related to vasovagal symptoms, further research is required to better understand the process.

Vasovagal Reactions During Blood Donation.

The blood donation setting provides and interesting context for investigating vasovagal syncope. While individuals who have a clinical phobia of needles or blood are not likely to present to such a clinic, research has both shown that needle fears are prevalent and that people donate blood for a variety of reasons (Gillespie & Hillyer, 2002; Sojka & Sojka, 2008). Thus, although they are volunteers, not all blood donors are totally at ease with the situation. Estimates have shown that between 1-15% of donors faint during blood donation depending on variables such as age and experience (Accurso et al., 2001). Although the overall rate is low, the likelihood that a first-time donor will experience a milder vasovagal reaction is much more likely, occurring in approximately 20% of donors (Ditto, France, Lavoie, Roussos, & Adler, 2003). While the levels of fainting are highest in first-time donors, these levels do not immediately drop off. Rates of syncopal occurrences only stabilize after about the 4th donation (Kasprisin, Glynn, Taylor, & Miller, 1992). Mild presyncopal symptoms include nausea, dizziness, sweating, and skin pallor. In one study using the Blood Donation Reactions Inventory, a self-report measure of 11 common blood donation symptoms, 69% of young inexperienced (but not necessarily novice) donors reported at least a mild experience of at least one symptom (Ditto, France, et al., 2003). Thus, while vasovagal reactions to blood donation range in severity, they are quite common.

While the blood loss inherent in donation certainly contributes to symptoms, it has been known for many years (e.g., Graham, 1961) that it is not the key element. For example, clinics require that donors be in good general health, at least 18 years old (or 16, depending on the jurisdiction), and meet other requirements related to weight and time between consecutive blood donations. As well, only about 10% total blood volume (450 mL) is withdrawn. This ensures that blood loss should not have any significant health impact and will be replenished quickly (Canadian Blood Services, 2010). Further, if blood loss was the only factor that produced reactions, every successful / full donation should produce symptoms.

Anxiety is probably the key determinant as suggested by the fact that reactions are almost unheard of among very experienced donors. Blood donation experience has often been found to be a significant predictor of reactions, along with age, predonation HR, and donor ratings of anxiety and fear (Ditto & France, 2006; France et al., 2011; Graham, 1961; Kasprisin et al., 1992; Meade, France, & Peterson, 1996; Newman, 1997). Individuals who report higher levels of BII fear or anxiety are more likely to experience vasovagal symptoms (Kleinknecht & Thorndike, 1990; Meade et al., 1996).

In general, blood donation clinics are well-positioned to treat vasovagal syncope and milder vasovagal reactions. There is a large concentration of trained personnel (in Canada, blood draws are conducted by nurses), donors give blood on reclining chairs, food and drink are available afterward, etc. However, reactions still pose problems. Reactions are medical events that require time to treat and document. Donors who react, and those who may seem to have

uneventful procedures, need to be monitored afterward to prevent or treat injury due to falls. Risks of hematomas, arterial puncture, and injury due to falls are involved and these all increase if the individual experiences vasovagal symptoms (Rubenstein & Josephson, 2002). Indeed, though extremely rare, there is a small mortality rate associated with blood donation vasovagal reactions (Brignole et al., 2004) underscoring the fact that this is a medical emergency. As a result it is common practice to halt the blood donation process once an individual begins experiencing symptoms to initiate treatment.

This has another effect in terms of the blood that has already been collected. Blood donation bags come equipped with a preset balance of chemicals that is prepared for a particular quantity of blood. If the donation is not completed because the needle must be removed due to a vasovagal reaction, the anticoagulant chemicals will not be correctly dosed in proportion to blood, causing the donation to be unusable.

But perhaps the greatest problem produced by vasovagal reactions, from the perspective of blood collection, is the fact that donors who react often do not return to give blood. A number of studies (Ditto & France, 2006; France, France, Roussos, & Ditto, 2004; Thomson et al., 1998) have documented the link between blood donation-related anxiety or vasovagal symptoms and reduced donor return, further emphasizing the necessity for research into the triggers of VVS and possible interventions to be implemented in blood clinics. Donors' subjective perceptions of symptoms, even mild ones, are a strong predictor of subsequent blood donations (France et al., 2004). Reports of mild symptoms, anxiety and distress in donors who faint are much greater than those that do not experience negative sequelae during their donations (Deacon & Abramowitz, 2006). These considerations support the need for the development of interventions to reduce vasovagal reactions in the blood clinic and elsewhere.

Classifying Blood Donation Reactions

Blood donation reactions became an area of interest for research in the 1960s. As reactions were noted increasingly in the literature, classification schemes were created. One of the first was developed by Williams and colleagues (Graham, 1961). This "grade of faint" scale simply categorized the level of syncope using three levels: 1 (feeling of faintness with no loss of consciousness), 2 (loss of consciousness for a short time) or 3 (prolonged loss of consciousness or short loss of consciousness with severe after effects). The American Red Cross followed suit and developed an internal classification system for donation reactions which was slightly more complex. They classify all donations into one of four categories: no reaction, mild reaction, moderate reaction and severe reaction (Newman, 1997). Light reactions may include lightheadedness, sighing, yawning, body temperature changes, perspiration, small or brief drop in heart rate, etc., or loss of consciousness for less than one minute. Moderate reactions include one or more symptoms from the light reaction and at least one of vomiting or severe nausea, large or sustained drop in heart rate, loss of bladder or bowel control or loss of consciousness for more than one minute. Severe reactions include one or more of the light or moderate reactions in addition to at least one or more of the following symptoms: sudden or large drop in blood pressure, chest pain, convulsions, rigidity, tremors, or cyanosis. While this system serves to differentiate the more severe reactions from the mild, it does not

permit comparison and differentiation of mild reactions that occur more commonly in the blood donation setting.

In the 1990's, Page developed the Blood Injection Symptom Scale (BISS) which was designed to measure symptoms elicited by blood and injection stimuli. The blood and injection symptoms that it measures fall within three categories: faintness, anxiety and tension. This nine item scale identifies faintness symptom clusters associated with situations involving blood and injections (Page, Bennett, Carter, Smith, & Woodmore, 1997). Participants respond Yes or No. Answers are summed to generate a faintness factor ranging from 0 to 9. This scale has good reported reliability with internal consistency (alpha coefficient = 0.85). While a strong point of this scale is the self-assessment of reported symptoms, the BISS has two shortcomings. First, responses are dichotomous and taken together; this subscale does not provide richness in data on severity of vasovagal symptoms. The donor who experiences several mild symptoms will not be differentiated well from the donor experiencing several severe symptoms. Secondly, the scale is designed to measure symptoms associated with phobic responses in blood and injection situations, not vasovagal symptoms per se. At first glance, it may appear that this would be appropriate for the blood donation setting however it may less applicable than it appears The blood donation setting is compromised of individuals whose presence is entirely voluntary. If a donor has phobic tendencies, it would follow that they would likely avoid the donation setting altogether and not engage in voluntary behaviours involving needles.

Blood Donation Reaction Inventory.

At the same time Page developed the BISS, Meade and France developed the Blood Donations Reaction Inventory (BDRI) (Meade et al., 1996). The BDRI is an 11-item inventory administered after blood donation. It assesses subjective physiological reactions such as fainting, dizziness and weakness. Participants rate their symptoms on a 6-point Likert scale ranging from 0 (not at all) to 5 (extremely) and the scores are summed to provide a total score ranging from 0 to 55. The reliability of this scale has been established (Ditto, France, et al., 2003) (Cronbach's a = 0.92) and it has been widely used in blood donation research (Bonk, France, & Taylor, 2001; Labus, France, & Taylor, 2000; Olatunji, Etzel, & Ciesielski, 2010). In addition to assessing subjective reactions, it strongly correlates with an objective measures of vasovagal reactions such as nurse initiated chair recline (France et al, 2004). Page and colleagues (1997) compared the BDRI to the BISS and found that the full version of the BDRI measures 2 factors similar to those found in the BISS: anxiety and tension. However, they also found that a weakness of the BDRI being that the total 11-item score correlates weakly with past history of fainting (Page et al., 1997). Further examination of this scale reveals that the BDRI is probably best used in a short form. The scale fit improves with fewer items; faintness, dizziness, weakness and lightheadedness being the strongest (France, Ditto, France, & Himawan, 2008). This version of the scale exhibits strong internal consistency reliability (Cronbach's $\mathbf{1} = 0.93$ to 0.96) and construct validity. Additionally, it is sensitive to different intensities of blood donation reactions, particularly mild, prefaint symptoms (France, Ditto, et al., 2008; France et al., 2011) addressing shortcomings of previous measures. Moreover, the scale is designed for use in the
general population, not only phobics, making it much more suitable for the blood donation setting, with individuals who voluntarily undergo venipuncture.

Applied Tension

One measure that seems to decrease vasovagal reactions in blood donors is Applied Muscle Tension (AT). AT is a behavioural technique developed by Öst and Sterner (1987) that involves tensing and releasing major muscles of the body, namely the arm and leg muscles while maintaining steady breathing. They introduced it as a potential treatment for fainting responses in BII phobics. This repeated tensing may prevent the rapid drop in blood pressure that occurs during vasovagal reactions in some individuals (Vögele et al., 2003). This may explain AT's ability to prevent vasovagal symptoms and syncope.

This intervention has proven to be effective in reducing vasovagal reactions in both BII phobics and non-fearful individuals exposed to medical stimuli (Foulds, Wiedmann, Patterson, & Brooks, 1990). In a laboratory investigation of AT, Foulds and colleagues found that both cerebral blood flow velocity and heart rate were increased in blood phobics and non-phobics. These changes were greater in those practicing AT than a distraction control group who was practicing mental arithmetic. On a similar note, Kowalsky and colleagues (2011) investigated whether cerebral oxygenation mediates the relationship between AT and attenuation of vasovagal symptoms in the blood donation clinic. They found that cerebral oxygenation decreased in a distraction-control group and that this decrease was attenuated in blood donors practicing AT. These results suggest that AT may be effective in part through increased availability of oxygen to the brain. Despite the "face validity" of the argument that AT reduces vasovagal symptoms by producing exercise-related increases in cardiovascular activity, (Hellstrom, Fellenius, & Öst, 1996) there may also be psychological processes at work. Supporting this idea, thought developed primarily as an adjunct therapy for exposure treatment, Öst and colleagues soon realized it was an effective "stand alone" treatment for BII (Öst, Sterner & Fellenius, 1989; Öst, Fellenius, & Sterner, 1991). Others suggest that the availability of a simple, plausible coping mechanism (AT) to practice may be the key factor in reducing the anxiety that initially triggered fainting (France, Montalva, France, & Trost, 2008), not its physiological impact. Furthermore, AT has been recommended for a variety of anxiety related problems (Antony & Swinson, 2000). Still, especially in the blood donor context, the prevailing view is that AT works primarily through exercise-related cardiovascular activity.

In the blood donation context, AT appears to decrease self-reported symptoms such as dizziness and nausea, reduce the need for chair reclining by phlebotomists, and an increase the likelihood of obtaining a full unit of blood (Ditto & France, 2006; Ditto, France, et al., 2003; Ditto, Wilkins, France, Lavoie, & Adler, 2003). However, AT does not appear to be equally effective for all individuals. For example, there may be differences in how females and males respond to AT. In a study by Ditto, France, Lavoie, Roussos, and Adler (2003), females who practiced AT had significantly fewer self-reported symptoms, chair reclines and were more likely to complete the donation than both females in a control condition and females who practiced a placebo version of Applied Tension. Participants in the placebo group only practiced Applied Tension from

the point when they sat in the donation chair to the time that the needle was inserted into their arm, a very brief period. The Applied Tension group practiced the technique before the needle was inserted as well as during the entire blood collection procedure. The number and intensity of negative symptoms were not related to body mass index or body weight, indicating that the effects of AT on females and males do not vary because of increased blood flow with the practice of AT in females due to a smaller body and blood supply. These findings suggest there is another factor playing a role in this differential effect of AT on females as compared to males.

In an attempt to further understand why AT has varying results, a subsequent study was performed to look at the specific components that may be responsible for the effectiveness of AT (Ditto, France, Albert, & Byrne, 2007). They noted that although AT appears to be a very physiological intervention, other processes such as expectancies may be involved in its effectiveness. That said, they found that a placebo group (who repeatedly squeezed and released only the arm with the needle, something commonly requested during normal donation) did not differ from a no-treatment group. However, they also found fewer blood donation-related symptoms in participants who received distraction instructions combined with upper body AT as compared to a similar AT group with no distraction. Unfortunately, it is difficult to study such issues, e.g., the relative importance of physiological change vs. anxiety reduction, in clinical studies of AT.

As a result, it is also important to conduct research on Applied Tension in a controlled laboratory environment. While clinical research provides insight to

donor reactions in the actual donation setting it is not conducive to more sophisticated physiological measurements that could enable a better understanding of the mechanisms behind fainting in the blood donation setting. Öst and colleagues (Öst, et. al., 1991; Öst, Lindahl, Sterner, & Jerremalm, 1984; Öst & Sterner, 1987; Öst, Sterner, et al., 1984) provide good descriptions of the basic processes at work. However, more detailed research investigating the physiological processes that occur with vasovagal symptoms are needed as well as research that uses stimuli resembling the blood donation setting. While it is well established that the tilt table can provoke a syncopal episode, particularly in those vulnerable to fainting, it is mismatch of stimuli as compared to one relating to blood, needles and injections.

Vögele and colleagues (2003) conducted a study of individuals fearful of blood focussing on blood pressure and heart rate responses to a video depicting open heart surgery. They compared physiological responses of participants practicing AT with a control group. They found that individuals who faint displayed a diphasic response while viewing the film but that AT attenuated this response. This study provided important understanding of AT as a treatment of vasovagal symptoms but it was lacking in more elaborate psychological measurements. Electrocardiogram measurements provide an understanding of the components of heart rate variability that are attributable to sympathetic and syncopal processes, the physiological side of syncope. In combination with psychological measurements and reports, these physiological data can help elucidate the processes at work and their timing with vasovagal symptoms and

syncope. In order to elucidate through which processes Applied Tension is effective, it is important to also consider the physiological measurements.

The studies presented in this attempt to address the methodological issues and shortcomings of previous research. Manuscript One presents a laboratory based investigation of Applied Tension. Participants watched a film clip of a simple venipuncture. Physiological and psychological measurements (questionnaires) were used to examine whether Applied Tension reduced vasovagal symptoms and, if so, if this was related more to changes in anxiety or cardiovascular change. Manuscript Two presents an extension of this research in a more clinical context, investigating AT in a randomized clinical trial. Given that anxiety is at work well before the actual blood donation takes place, the second study examined mechanisms through which Applied Tension works in part by having participants practice AT at different times; before and / or during blood donations. In using Applied Tension at different moments, it enabled the investigation of whether Applied Tension is works primarily by maintaining cardiovascular activity vs. addressing psychological processes leading up to blood donation.

References

Accurso, V., Winnicki, M., Shamsuzzaman, A. S. M., Wenzel, A., Johnson, A.
K., & Somers, V. K. (2001). Predisposition to vasovagal syncope in subjects with blood/injury phobia. *Circulation, 104*(8), 903-907. doi: 10.1161/hc3301.094910

Antony, M. M., & Swinson, R. P. (2000). *Phobic disorders and panic in adults: A guide to assessment and treatment*. Washington, DC: American Psychological Association.

Berntson, G. G., Norman, G. J., Hawkley, L. C., & Cacioppo, J. T. (2008).
Cardiac autonomic balance versus cardiac regulatory capacity. *Psychophysiology*, 45(4), 643-652.
doi: 10.1111/j.1469-8986.2008.00652.x

- Bonk, V. A., France, C. R., & Taylor, B. K. (2001). Distraction reduces selfreported physiological reactions to blood donation in novice donors with a blunting coping style. *Psychosomatic Medicine*, 63(3), 447-452.
- Bracha, H. S. (2004). Freeze, flight, fight, fright, faint; Adaptationist perspectives on the acute stress response spectrum. *CNS Spectrums*, *9*(9), 679-685.
- Bracha, H. S., Bracha, A. S., Williams, A. E., Ralston, T. C., & Matsukawa, J. M. (2005). The human fear-circuitry and fear-induced fainting in healthy individuals. *Clinical Autonomic Research*, *15*(3), 238-241.
 doi: 10.1007/s10286-005-0245-z
- Brignole, M., Alboni, P., Benditt, D. G., Bergfeldt, L., Blanc, J. J., Thomsen, P. E.
 B., et al. (2004). Guidelines on management (diagnosis and treatment) of syncope Update 2004. *European Heart Journal*, 25(22), 2054-2072.

doi: 10.1016/j.ehj.2004.09.004

Brown, H., & McCormack, P. (1942). An analysis of vasomotor phenomena (faints) occurring in blood donors. *British Medical Journal*, 1(4226), 1-5.

Busch, M. P., Guiltinan, A., Skettino, S., Cordell, R., Zeger, G., & Kleinman, S. (1991). Safety of blood donations following a natural disaster. *Transfusion*, 31(8), 719-723.
doi: 10.1046/j.1537-2995.1991.31892023497.x

- Custer, B., Johnson, E. S., Sullivan, S. D., Hazlet, T. K., Ramsey, S. D., Hirschler, N. V., et al. (2004). Quantifying losses to the donated blood supply due to donor deferral and miscollection. *Transfusion*, 44(10), 1417-1426. doi: 10.1111/j.1537-2995.2004.04160.x
- D'Antono, B., Dupuis, G., St-Jean, K., Lévesque, K., Nadeau, R., Guerra, P.,
 Thibault, B., & Kus, T. (2009). Prospective evaluation of psychological distress and psychiatric morbidity in recurrent vasovagal and unexplained syncope. *Journal of Psychosomatic Research*, 67(3), 213-222. doi: 10.1016/j.jpsychores.2009.03.012

Davey, R. J. (2004). Recruiting blood donors: Challenges and opportunities. *Transfusion*, 44(4), 597-600. doi: 10.1111/j.0041-1132.2004.04402.x

- Deacon, B., & Abramowitz, J. (2006). Fear of needles and vasovagal reactions among phlebotomy patients. *Journal of Anxiety Disorders*, 20(7), 946-960.
 doi: 10.1016/j.janxdis.2006.01.004
- Dermkasian, G., & Lamb, L. E. (1958). Syncope in a population of healthy young adults. *Journal of the American Medical Association*, *168*, 1200-1207.
 doi: 10.1001/jama.1958.03000090030007

- Diehl, R. (2005). Vasovagal syncope and Darwinian fitness. *Clinical Autonomic Research*, *15*(2), 126-129. doi: 10.1007/s10286-005-0244-0
- Ditto, B., Balegh, S., Gilchrist, P. T., & Holly, C. D. (2011). Relation between perceived blood loss and vasovagal symptoms in blood donors. *Clinical Autonomic Research, Online First.* doi: 10.1007/s10286-011-0147-1
- Ditto, B., & France, C. R. (2006). Vasovagal symptoms mediate the relationship between predonation anxiety and subsequent blood donation in female volunteers. *Transfusion*, 46(6), 1006-1010. doi: 10.1111/j.1537-2995.2006.00835.x
- Ditto, B., France, C. R., Albert, M., & Byrne, N. (2007). Dismantling applied tension: Mechanisms of a treatment to reduce blood donation-related symptoms. *Transfusion*, 47(12), 2217-2222.
 doi: 10.1111/j.1537-2995.2007.01449.x
- Ditto, B., France, C. R., Lavoie, P., Roussos, M., & Adler, P. S. (2003). Reducing reactions to blood donation with applied muscle tension: a randomized controlled trial. *Transfusion*, 43(9), 1269-1275.
 doi : 10.1046/j.1537.2995.2003.00488.x
- Ditto, B., Wilkins, J. A., France, C. R., Lavoie, P., & Adler, P. S. (2003). On-site training in applied muscle tension to reduce vasovagal reactions to blood donation. *Journal of Behavioral Medicine*, *26*(1), 53-65.
 doi: 10.1023/A:1021795022380
- Drackley, A., Newbold, K. B., Paez, A., & Heddle, N. (2011). Forecasting
 Ontario's blood supply and demand. *Transfusion*, *Online First*.
 doi: 10.1111/j.1537-2995.2011.03280.x

- Engel, G. L. (1978). Psychologic stress, vasodepressor (vasovagal) syncope, and sudden death. *Annals of Internal Medicine*, 89(3), 403-412.
- Ferguson, E., France, C. R., Abraham, C., Ditto, B., & Sheeran, P. (2007).
 Improving blood donor recruitment and retention: integrating theoretical advances from social and behavioral science research agendas. *Transfusion, 47*(11), 1999-2010. doi: 10.1111/j.1537-2995.2007.01423.x
- Foulds, J., Wiedmann, K., Patterson, J., & Brooks, N. (1990). The effects of muscle tension on cerebral circulation in blood-phobic and non-phobic subjects. *Behaviour Research and Therapy*, 28(6), 481-486. doi: 10.1016/0005-7967(90)90134-5
- France, C. R., Ditto, B., France, J. L., & Himawan, L. K. (2008). Psychometric properties of the Blood Donation Reactions Inventory: a subjective measure of presyncopal reactions to blood donation. *Transfusion*, 48(9), 1820-1826. doi: 10.1111/j.1537-2995.2008.01831.x
- France, C. R., France, J. L., Kowalsky, J. M., Ellis, G. D., Copley, D. M., Geneser, A., et al. (2011). Assessment of donor fear enhances prediction of presyncopal symptoms among volunteer blood donors. *Transfusion*, *Online First*. doi: 10.1111/j.1537-2995.2011.03294.x
- France, C. R., France, J. L., Roussos, M., & Ditto, B. (2004). Mild reactions to blood donation predict a decreased likelihood of donor return. *Transfusion* and Apheresis Science, 30(1), 17-22. doi: 10.1016/j.transci.2003.08.014
- France, C. R., Montalva, R., France, J. L., & Trost, Z. (2008). Enhancing attitudes and intentions in prospective blood donors: evaluation of a new donor recruitment brochure. *Transfusion*, 48(3), 526-530.

doi: 10.1111/j.1537-2995.2007.01565.x

- Ganzeboom, K. S., Colman, N., Reitsma, J. B., Shen, W. K., & Wieling, W.
 (2003). Prevalence and triggers of syncope in medical students. *The American Journal of Cardiology*, *91*(8), 1006-1008.
 doi: 10.1016/S0002-9149(03)00127-9
- Germain, M., Decary, F., Chiavetta, J., & Goldman, M. (2000). Variant Creutzfeldt-Jakob disease and the Quebec blood supply. *The Canadian Medical Association Journal*, 163(4), 412-413.
- Gillespie, T. W., & Hillyer, C. D. (2002). Blood donors and factors impacting the blood donation decision. *Transfusion Medicine Reviews*, 16(2), 115-130. doi: 10.1053/tmrv.2002.31461
- Glynn, S. A., Busch, M. P., Schreiber, G. B., Murphy, E. L., Wright, D. J., Tu, Y., et al. (2003). Effect of a national disaster on blood supply and safety. *JAMA: The Journal of the American Medical Association*, 289(17), 2246-2253. doi: 10.1001/jama.289.17.2246
- Godin, G., Sheeran, P., Conner, M., Germain, M., Blondeau, D., Gagné, C., et al. (2005). Factors explaining the intention to give blood among the general population. *Vox Sanguinis*, 89(3), 140-149.
 doi: 10.1111/j.1423-0410.2005.00674.x
- Graham, D. T. (1961). Prediction of fainting in blood donors. *Circulation, 23*, 901-906. doi: 10.1161/01.CIR.23.6.901
- Graham, D. T., Kabler, J. D., & Lunsford, L. J. (1961). Vasovagal fainting: A diphasic response. *Psychosomatic Medicine*, 23(6), 493-507.

- Greenbury, C. L. (1942). An analysis of the incidence of "fainting" in 5,897 unselected blood donors. *British Medical Journal*, 1(4233), 253-255.
- Growers, W. R. (1907). A lecture on vagal and vasovagal attacks. *Lancet, 1907*, 1551-1553.
- Hellstrom, K., Fellenius, J., & Öst, L. G. (1996). One versus five sessions of applied tension in the treatment of blood phobia. *Behavior Research and Therapy*, 34(2), 101-112. doi: 0005-7967(95)00060-7
- Kasprisin, D. O., Glynn, S. H., Taylor, F., & Miller, K. A. (1992). Moderate and severe reactions in blood donors. *Transfusion*, 32(1), 23-26.
 doi: 10.1046/j.1537-2995.1992.32192116426.x
- Klein, H. G., & Anstee, D. J. (2007). Blood donors and the withdrawal of blood.
 In P. M. Ness & R. S. Shirey (Eds.), *Mollison's Blood Transfusion in Clinical Medicine* (11th ed., pp. 1-18): Blackwell Science Ltd.
- Kleinknecht, R. A., & Lenz, J. (1989). Blood/injury fear, fainting and avoidance of medically-related situations: a family correspondence study. *Behaviour Research and Therapy*, 27(5), 537-547.

doi: 10.1016/0005-7967(89)90088-0

- Kleinknecht, R. A., & Thorndike, R. M. (1990). The Mutilation Questionnaire as a predictor of blood/injury fear and fainting. *Behaviour Research and Therapy*, 28(5), 429-437. doi: 10.1016/0005-7967(89)90088-0
- Kleinknecht, R. A., Thorndike, R. M., & Walls, M. M. (1996). Factorial dimensions and correlates of blood, injury, injection and related medical fears: Cross validation of the Medical Fear Survey. *Behaviour Research and Therapy*, 34(4), 323-331. doi: 10.1016/0005-7976(95)00072-0

- Kowalsky, J. M., France, J. L., Wissel, M. E., & France, C. R. (2011). Effect of applied muscle tension on cerebral oxygenation in female blood donors. *Transfusion*, *51*(8), 1802-1808. doi: 10.1111/j.1537-2995.2011.03075.x
- Labus, J., France, C., & Taylor, B. (2000). Vasovagal reactions in volunteer blood donors: Analyzing the predictive power of the medical fears survey. *International Journal of Behavioral Medicine*, 7(1), 62-72.
 doi: 10.1207/s15327558ijbm0701_5
- Lamb, L. E., Green, H. C., & Combs, J. J. (1960). Incidence of loss of consciousness in Air Force personnel. *Aerospace Medicine*, 12, 973-988.
- Lewis, T. (1932). A lecture on vasovagal syncope and the carotid sinus mechanism. *British Medical Journal*, *1*, 837-876.
- Linden, J. V., Gregorio, D. I., & Kalish, R. I. (1988). An estimate of blood donor eligibility in the general population. *Vox Sanguinis*, 54(2), 96-100.
 doi: 10.1111/j.1423-0410.1988.tb01624.x
- Masser, B. M., White, K. M., Hyde, M. K., & Terry, D. J. (2008). The psychology of blood donation: current research and future directions. *Transfusion Medicine Reviews*, 22(3), 215-233. doi: 10.1016/j.tmrv.2008.02.005
- McCullough, J. (1993). The nation's changing blood supply system. *Journal of the American Medical Association*, 269(17), 2239-2245.
 doi: 10.1001/jama.1993.03500170069036
- Meade, M. A., France, C. R., & Peterson, L. M. (1996). Predicting vasovagal reactions in volunteer blood donors. *Journal of Psychosomatic Research*, 40(5), 495-501. doi: 10.1016/0022-3999(95)00639-7

- Moore, R. J. (1991). Promoting blood donation: a study of the social profile, attitudes, motivation and experience of donors. *Transfusion Medicine*, *1*(4), 201-207. doi : 10.1111/j.1365-3148.1991.tb00034.x
- Mosqueda-Garcia, R., Furlan, R., Tank, J., & Fernandez-Violante, R. (2000). The elusive pathophysiology of neurally mediated syncope. *Circulation*, 102(23), 2898-2906. doi: 10.1161/01.CI.102.23.2898
- Murdoch, B. D. (1980). Loss of consciousness in healthy South African men: Incidence, causes and relationship to EEG abnormality. *South African Medical Journal* 57(19), 771-774.
- Newman, B. H. (1997). Donor reactions and injuries from whole blood donation. *Transfusion Medicine Reviews*, *11*(1), 64-75. doi: 10.1016/s0887-7963(97)80011-9
- Olatunji, B. O., Etzel, E. N., & Ciesielski, B. G. (2010). Vasovagal syncope and blood donor return: examination of the role of experience and affective expectancies. *Behavior Modification*, *34*(2), 164-174. doi: 10.1177/0145445510362576
- Olatunji, B. O., Williams, N. L., Sawchuk, C. N., & Lohr, J. M. (2006). Disgust, anxiety and fainting symptoms associated with blood-injection-injury fears: a structural model. *Journal of Anxiety Disorders*, 20(1), 23-41. doi: 10.1016/j.janxdis.2004.11.009
- Öst, L. G., Fellenius, J., & Sterner, U. (1991). Applied tension, exposure in vivo, and tension-only in the treatment of blood phobia. *Behavior Research and Therapy*, 29(6), 561-574. doi: 0005-7967(91)90006-O

- Öst, L. G., Lindahl, I. L., Sterner, U., & Jerremalm, A. (1984). Exposure in vivo vs applied relaxation in the treatment of blood phobia. *Behavior Research and Therapy*, 22(3), 205-216. doi: 0005-7967(84)90001-9 [pii]
- Öst, L. G., & Sterner, U. (1987). Applied tension. A specific behavioral method for treatment of blood phobia. *Behavior Research and Therapy*, 25(1), 25-29. doi: 10.1016/0005-7967(87)90111-2
- Öst, L. G., Sterner, U., & Fellenius, J. (1989). Applied tension, applied relaxation, and the combination in the treatment of blood phobia. *Behaviour Research and Therapy*, 27(2), 109-121. doi: 10.1016/0005-7967(89)90069-7
- Öst, L. G., Sterner, U., & Lindahl, I. L. (1984). Physiological responses in blood phobics. *Behaviour Research and Therapy*, 22(2), 109-117. doi: 10.1016/0005-7967(84)90099-8
- Page, A. C. (1994). Blood-injury phobia. *Clinical Psychology Review*, *14*(5), 443-461. doi: 10.1016/0272-7358(94)90036-1
- Page, A. C. (2003). The role of disgust in faintness elicited by blood and injection stimuli. *Journal of Anxiety Disorders*, 17(1), 45-58.
 doi: 10.1016/s0887-6185(02)00169-x
- Page, A. C., Bennett, K. S., Carter, O., Smith, J., & Woodmore, K. (1997). The Blood-Injection Symptom Scale (BISS): Assessing a structure of phobic symptoms elicited by blood and injections. *Behaviour Research and Therapy*, 35(5), 457-464. doi: 10.1016/S0005-7967(96)00120-9
- Poles, F. C., & Boycott, M. (1942). Syncope in blood donors. *The Lancet*, 240(6219), 531-535. doi: 10.1016/s0140-6736(00)58098-2

- Reid, M., & Wood, A. (2008). An investigation into blood donation intentions among non-donors. *International Journal of Nonprofit and Voluntary Sector Marketing*, 13(1), 31-43. doi: 10.1002/nvsm.296
- Riley, W., Schwei, M., & McCullough, J. (2007). The United States' potential blood donor pool: Estimating the prevalence of donor-exclusion factors on the pool of potential donors. *Transfusion*, 47(7), 1180-1188.
 doi: 10.1111/j.1537-2995.2007.01252.x
- Ritz, T., Meuret, A. E., & Ayala, E. S. (2010). The psychophysiology of bloodinjection-injury phobia: looking beyond the diphasic response paradigm. *International Journal of Psychophysiology*, 78(1), 50-67. doi: 10.1016/j.ijpsycho.2010.05.007
- Rozin, P., & Fallon, A. E. (1987). A perspective on disgust. *Psychological Review*, 94(1), 23-41. doi: 10.1037/0033-295Z.94.1.23
- Ruetz, P. P., Johnson, S. A., Callahan, R., Meade, R. C., & Smith, J. J. (1967).Fainting: a review of its mechanisms and a study in blood donors.*Medicine*, 46(5), 363-384.
- Sawchuk, C. N., Lohr, J. M., Tolin, D. F., Lee, T. C., & Kleinknecht, R. A. (2000). Disgust sensitivity and contamination fears in spider and blood– injection–injury phobias. *Behaviour Research and Therapy*, 38(8), 753-762. doi: 10.1016/s0005-7967(99)00093-5
- Schreiber, George B., Glynn, Simone A., Damesyn, Mark A., Wright, David J., Tu, Y., Dodd, Roger Y., et al. (2003). Lapsed donors: an untapped resource. *Transfusion*, 43(1), 17-24. doi: 10.1046/j.1537-2995.2003.00290.x

- Schreiber, George B., Schlumpf, Karen S., Glynn, Simone A., Wright, David J., Tu, Y., King, Melissa R., et al. (2006). Convenience, the bane of our existence, and other barriers to donating. *Transfusion*, 46(4), 545-553. doi: 10.1111/j.1537-2995.2006.00757.x
- Services, C. B. (2009). A report to Canadians: 10 years later, A new mandate. Ottawa: Canadian Blood Services.
- Services, C. B. (2010). Basic Eligibility Can I donate? (Vol. 2010).
- Services, C. B. (2011). Who needs blood?
- Sheldon, R., Rose, S., Connolly, S., Ritchie, D., Koshman, M. L., Frenneaux, M., et al. (2005). Diagnostic criteria for vasovagal syncope based on a quantitative history. *European Heart Journal*. doi: 10.1093/eurheartj/ehi584
- Sojka, B. N., & Sojka, P. (2008). The blood donation experience: self-reported motives and obstacles for donating blood. *Vox Sanguinis*, 94(1), 56-63. doi: 10.1111/j.1423-0410.2007.00990.x
- Soteriades, E. S., Evans, J. C., Larson, M. G., Chen, M. H., Chen, L., Benjamin,
 E. J., et al. (2002). Incidence and prognosis of syncope. *The New England Journal of Medicine*, 347(12), 878-885. doi: 10.1056/NEJMoa012407
- Sullivan, M. T., Cotten, R., Read, E. J., & Wallace, E. L. (2007). Blood collection and transfusion in the United States in 2001. *Transfusion*, 47(3), 385-394. doi: 10.1111/j.1537-2995.2007.01128.x
- Taylor, E. S. (1942). Procurement of blood for the armed forces. *Journal of the American Medical Association*, *120*(2), 119-123.
 doi: 10.1001/jama.1942.82830370004009

- Thijs, R. D., Wieling, W., Kaufmann, H., & van Dijk, G. (2004). Defining and classifying syncope. *Clinical Autonomic Research*, 14(0), i4-i8.
 doi: 10.1007/s10286-004-1002-4
- Thomson, R. A., Bethel, J., Lo, A. Y., Ownby, H. E., Nass, C. C., & Williams, A. E. (1998). Retention of "safe" blood donors. The Retrovirus Epidemiology Donor Study. *Transfusion*, 38(4), 359-367.
 doi: 10.1046/j.1537-2995.1998.38498257374.x
- National Health Service Blood and Transplantation Unit, (2011). NHSBT sees surge in blood donors as almost 100,000 make a "Date to Donate".
- van Lieshout, J. J., Wieling, W., Karemaker, J. M., & Eckberg, D. L. (1991). The vasovagal response. *Clinical Science*, *81*(5), 575-586.

Vögele, C., Coles, J., Wardle, J., & Steptoe, A. (2003). Psychophysiologic effects of applied tension on the emotional fainting response to blood and injury. *Behaviour Research and Therapy*, *41*(2), 139-155.
doi: 10.1016S0005-7967(01)00133-4

- Williams, G. E. O. (1942). Syncopal reactions in blood donors. *British Medical Journal*, 1, 1-5.
- Wiwanitkit, V. (2005). Overview of the blood donation in acute post-Tsunami in Thailand. *Prehospital and Disaster Medicine*, 20(5), 350.
- Wolf, S. (1958). Cardiovascular reactions to symbolic stimuli. *Circulation*, *18*(2), 287-292. doi: 10.1161/01.CIR.18.2.287
- Wright, S., Yelland, M., Heathcote, K., Ng, S. K., & Wright, G. (2009). Fear of needles- Nature and prevalence in general practice. *Australian Family Physician*, 38(3), 172-176.

Zuck, T. F., Thomson, R. A., Schreiber, G. B., Gilcher, R. O., Kleinman, S. H.,
Murphy, E. L., et al. (1995). The Retrovirus Epidemiology Donor Study (REDS): rationale and methods. *Transfusion*, 35(11), 944-951. doi: 10.1046/j.1537-2995.1995.351196110900.x

MANUSCRIPT ONE

APPLIED TENSION AND BLOOD DOANTION SYMPTOMS: THE IMPORTANCE OF ANXIETY REDUCTION

Holly, C. D., Balegh, S., Ditto, B. (2011). Applied Tension and Blood Donation
Symptoms: The Importance of Anxiety Reduction. *Health Psychology*, 30(3). 320-325.

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Abstract

Objective: Despite being a voluntary activity, many blood donors experience anxiety and fainting (syncope) is not unusual. The muscle tensing technique Applied Tension (AT) has been found to be effective in reducing vasovagal symptoms and syncope. A series of studies was developed to investigate the role of AT on anxiety and fainting. Methods: The mechanisms of AT were examined in the laboratory and the blood donor clinic. In Study One, seventy participants were assigned randomly to either a control group or an experimental group who learned AT before watching a video depicting blood draws. In Study Two, 667 volunteer blood donors completed similar questionnaires. *Results:* In Study One, a significant Condition x Sex x Needle Fear interaction, F(1, 59) = 4.97, p = 0.03indicated that AT reduced vasovagal symptoms in higher fear females. Study Two also found a significant Condition x Sex x Needle Fear effect on vasovagal symptoms, F(2, 653) = 3.95, p = 0.020, indicating that AT reduced symptoms but primarily among females with more pronounced fears of needles. *Conclusions:* Analysis of the physiological data and self-report anxiety supports the conclusion that the reduction in vasovagal symptoms was due more to decreased anxiety rather than exercise-related cardiovascular change. These results suggest that AT may provide a useful means of coping with invasive medical procedures in part by reducing anxiety.

Keywords: Applied Tension, syncope, fainting, anxiety, blood donation.

Introduction

In many respects, the medical system hinges on volunteer blood donations. According to the American Red Cross, every two seconds someone is in need of blood. For many emergency and non-emergency medical procedures blood is a crucial resource. Unfortunately, less than 40% of the population is eligible to donate blood and only about 5% of these individuals volunteer each year (Gillespie & Hillyer, 2002). Further, many do not return to give blood another time. It has been estimated that up to half of all first-time donors do not give blood again (Ownby, Kong, Watanabe, Tu, & Nass, 1999). Health psychology has the potential to improve the blood supply by studying factors associated with the recruitment and retention of donors. For example, research shows that the occurrence of even mild symptoms such as dizziness and weakness during blood donation decreases donor return (France, France, Roussos, & Ditto, 2004).

Applied Tension (AT) is a behavioral technique that has been found to reduce dizziness and fainting in some contexts. It was developed by Öst in the eighties as an aid to behavioral exposure therapy for blood and injury phobias as so many people became dizzy or fainted during exposure, interrupting or terminating treatment (Hellstrom, Fellenius, & Öst, 1996; Öst, Fellenius, & Sterner, 1991; Öst & Sterner, 1987). The primary component is repeated isometric muscle tension, particularly in the arms and legs, which presumably maintains blood pressure in the face of vasovagal activity that would otherwise lead to decreases in blood pressure and cerebral perfusion. The intervention has proven to be effective in reducing vasovagal symptoms in both blood and injury phobics and non-phobic people undergoing medical procedures such as blood

donation (Ditto, Byrne, & Holly, 2009; Ditto & France, 2006; Ditto, Wilkins, France, Lavoie, & Adler, 2003).

While the muscle tension / exercise component of AT clearly increases blood pressure and the delivery of oxygen to the brain (Foulds, Wiedmann, Patterson, & Brooks, 1990; France, France, & Patterson, 2006) and AT has been found to stabilize cardiovascular activity in blood donors (Ditto et al., 2009) and laboratory volunteers watching a video of cardiac surgery (Vögele, Coles, Wardle, & Steptoe, 2003), growing evidence suggests that its effects on vasovagal symptoms may be due more to anxiety reduction than exercise-related cardiovascular activity. For example, AT appears to benefit female donors more than male donors, who generally report less anxiety (Ditto, France, Lavoie, Roussos, & Adler, 2003). We also recently found that a "placebo" version of AT significantly reduced symptoms (Ditto, France, Albert, & Byrne, 2007). In general, donors who tensed just their arms but not their legs did not have reduced symptoms. However, donors who were also asked, somewhat misleadingly, to focus more on the arm that did not have the needle in it in order to "develop a better sense of the amount of tension required" had fewer vasovagal symptoms and lower anxiety scores than the no treatment control group. Whether this condition is better viewed a distraction than placebo condition is difficult to say since, more broadly, it is difficult to study issues such as the relative importance of cardiovascular change vs. anxiety reduction in clinical studies of AT. As a result, one goal of the present research was to develop a laboratory analogue of the blood donation procedure. Another was to examine more closely the relative

roles of exercise-related cardiovascular activity vs. anxiety reduction in the effects of AT on vasovagal symptoms.

Following in the tradition of laboratory studies that used movies depicting surgery with blood and injury patients (Sarlo, Buodo, Munafo, Stegagno, & Palomba, 2008; Vögele et al., 2003), a less intense video displaying various blood draw procedures was shown to young adults who might be prospective blood donors. It was hypothesized that AT would reduce vasovagal symptoms primarily by reducing anxiety. As a result, the main beneficiaries were expected to be people with higher pre-experiment scores on a questionnaire reflecting anxiety about needles. The laboratory environment also allowed collection of physiological measures such as blood pressure, heart rate, and heart rate variability to clarify the mechanisms of AT.

Study One

Method.

Participants.

Seventy healthy young adults were recruited via campus advertisements. To eliminate people with extensive blood donation experience, potential participants were screened for prior blood donation and excluded if they had given blood more than five times in their life. Additional exclusion criteria included medical illness (i.e., asthma, cardiovascular issues, vision or hearing problems), psychological disturbances (i.e., depression, anxiety), and use of medications that might influence cardiovascular activity.

Three of the 70 participants experienced vasovagal symptoms that were severe enough to interfere with data collection (though no clear faints occurred).

As a result, analyses were conducted on data obtained from 67 individuals (35 females, 32 males) aged 18 to 30 years, (M = 22.8, SD = 3.29). Seventeen males and 17 females were assigned randomly to the treatment (Applied Tension) group, the others to a no treatment control group. Participants were reimbursed \$20 CAD for their time. The research was approved by the McGill University Institutional Research Board.

Apparatus.

A Biopac MP35 System was used to obtain continuous measures of interbeat interval (IBI; heart rate) and skin conductance (SC). The ECG electrodes were placed bilaterally on the lower ribcage and on the ankle. Electrodes were placed on the non-dominant index and middle fingertips to measure SC. Measurements of systolic and diastolic blood pressure (SBP, DBP) were obtained periodically using a Datascope Accutorr Plus automatic monitor.

BSL Pro 3.7.3 software was used to collect the Biopac data. Heart rate variability was assessed using HRV Analysis Software (Biomedical Signal Analysis Group, Department of Applied Physics, University of Kuopio, Finland). Once abnormal heartbeats and artefacts were removed, a frequency domain analysis was conducted on the data. Analysis of the heart rate variability spectrum reveals a high-frequency (HF; 0.15 - 0.40 HZ), a low frequency (LF; 0.04 - 0.15 HZ), and very low-frequency components. The high-frequency peak is a reliable indicator of parasympathetic (vagal) activity. The autonomic origins of low-frequency HRV are more ambiguous, including both sympathetic and parasympathetic activity. However, the ratio of low- to high-frequency HRV is often used as an index of cardiac sympathetic activity (Task Force of the

European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996).

Participants learned AT by watching a 2-minute instructional video used in previous research (Ditto et al., 2009). The blood donation stimulus was a 28min medical instruction video titled Basic Venipuncture created by the Center for Phlebotomy Education. A number of venipunctures are displayed along with discussion of proper techniques and problems that can occur during the procedure.

Questionnaires.

Participants completed a number of questionnaires both before and after viewing the film. Prior to the film, the participants completed a demographic questionnaire and the Medical Fears Survey (Kleinknecht, Thorndike, & Walls, 1996). Fear of a number of medical procedures was rated on a five-point Likert scale ranging from 0 (no fear at all) to 4 (terror). A needle fear score was computed by summing 10 items related to fear of needles. Participants also completed the Spielberger State Anxiety Inventory (STAI) (Spielberger, Gorsuch, & Edward, 1970) at the beginning and end of the study. The STAI is a 20-item self-report scale where various mood statements are rated on a five-point Likert scale ranging from 1 (not at all) to 4 (very much). Finally, the Blood Donation Reaction Inventory (BDRI; (Meade, France, & Peterson, 1996) was completed after viewing the film. The BDRI assesses severity of 11 common vasovagal symptoms on a six-point Likert scale ranging from 0 (not at all) to 5 (to an extreme degree). We used the recently recommended factor analysis-based scoring scheme focusing on four key items (dizziness, faintness, weakness, lightheadedness) (France, Ditto, France, & Himawan, 2008).

Procedure.

After obtaining informed consent participants were given the first set of questionnaires to complete. Subsequently, the physiological recording apparatus was attached. The body of the study consisted of 10 5-minute intervals in which participants were asked to perform certain tasks. In Section 1 (segments 1-3) all participants began by resting for five minutes to allow baseline physiological data to be collected. Afterwards, those assigned to the AT group learned and practiced Applied Tension for 10 minutes while the others continued to sit quietly. AT involves gentle repeated whole body isometric tension in 5-s on, 5-s off cycles while maintaining steady breathing. Section 2 began with another five-minute rest period (segment 4) followed by watching the video, Basic Venipuncture (segments 5-10). Participants who had learned AT were asked to practice it while watching the movie. Following the video, all participants completed the BDRI and the STAI. Anyone reporting or displaying signs of a vasovagal reaction was asked to remain in the laboratory until symptoms passed. ECG and SC measurements were obtained continuously during the protocol. Two measurements of blood pressure were obtained during the initial baseline period (segment 1), while participants were practicing AT or resting (segment 3), the pre-video rest period (segment 4), and during the most dramatic part of the video (segment 9).

Data Reduction and Analysis.

Mean values of IBI and SC were calculated for each 5-minute block as well as estimates of HF HRV and the LF/HF ratio. Mean values of SBP and DBP were calculated for the initial baseline, Applied Tension, pre-video rest and video

periods. The primary analyses were general linear models (GLM) as they can accommodate both categorical and continuous independent variables. In most analyses sex and condition (AT or no AT) were included as independent variables along with needle fear score as a continuous variable. To assess the effects of Applied Tension on most of the (non blood pressure) physiological measures before the venipuncture video, a repeated measure of Time with three levels was added to the GLM (segments 1-3). To assess the effects of Applied Tension on response to the video, a repeated measure of Time with seven levels (pre-video rest + video periods) was added. The Greenhouse-Geisser correction was used in tests of repeated measures involving more than two levels.

Results.

The Effects of Applied Tension on Vasovagal Symptoms / Manipulation Check.

While the BDRI is a well-validated measure of vasovagal symptoms, several preliminary analyses were conducted to examine its physiological correlates. Most notably, a 2 Time (before/during video) x BDRI (considered as a continuous variable) GLM of systolic blood pressure levels revealed a Time x BDRI interaction, F(1,63) = 7.52, p = 0.008, indicating a significant decrease in SBP during the video among those who reported vasovagal symptoms.

The Condition x Sex x Needle Fear GLM of the BDRI scores also supported the validity of scores in that a strong main effect of Needle Fear score, F(1,59) = 14.56, p < 0.001, was observed. That is, people who indicated being more fearful of needles before the experiment reported significantly more dizziness, etc. following the video depicting a number of blood draws. More important to the purpose of the experiment, the Condition x Sex x Needle Fear interaction was significant, F(1, 59) = 4.97, p = 0.03. As can be seen in Figure 1 (which for purposes of illustration divides participants on the median of needle fear) this interaction was due to trends within females. Separate Condition x Needle Fear GLMs for males and females revealed only a main effect of Needle Fear in males, F(1,28) = 8.33, p = 0.007. In contrast, the Condition x Needle Fear interaction was significant in females, F(1,31) = 5.96, p = 0.021. AT reduced vasovagal symptoms in females but only among those with higher needle fear. This suggests anxiety reduction may have been involved although on the other hand females with lower needle fear had few symptoms to begin with. Was the change in vasovagal symptoms associated with exercise-related cardiovascular activity?

Physiological Measures.

Effects of Applied Tension on physiological activity before the venipuncture video.

The GLM of interbeat intervals in segments 1-3 produced a main effect of Sex, due to generally smaller interbeat intervals (higher heart rate) among females, F(1,57) = 6.19, p = 0.016, but more important a significant Condition x Time interaction, F(2,114) = 9.93, p = 0.001 (Figure 2). That is, Applied Tension produced the expected increase in heart rate. There were no significant effects in the analyses of pre-video SBP, DBP, or HF HRV. However, similar to IBI, the Condition x Time interaction was significant in the analysis of the low frequency/high frequency ratio, F(2,104) = 3.52, p = 0.035. The ratio increased among those who practiced AT, suggesting that their increase in heart rate was partially sympathetically mediated. Similarly, the GLM of skin conductance produced an interesting Time x Needle Fear x Condition interaction, F(2,114) =3.89, p = 0.036. In general, skin conductance increased as people practiced AT, providing further evidence that their increase in heart rate was at least partially sympathetically-mediated. However, the increase in SC was particularly marked among participants with higher needle fear, suggesting stressful anticipation of the upcoming venipuncture video.

Effects of the venipuncture video and Applied Tension.

Similar to the GLM of IBI values when people were learning and practicing AT, the analysis of values just before and during the video (segments 4-10) produced a main effect of Sex, F(1,53) = 4.90, p = 0.031, as well as a significant Condition x Time interaction, F(6,318) = 3.83, p = 0.006. Heart rate went up when people started to do AT. Importantly, sex did not interact with condition and males and females who practiced AT experienced similar increases in heart rate. Thus, muscle tensing-induced heart rate acceleration per se cannot explain fewer symptoms in female participants. Once again, the Condition x Time interaction was significant in the GLM of skin conductance, F(6,318) =2.90, p = 0.028, due to a greater increase in people who practiced AT. LF/HF ratios were similar, producing a main effect of Condition, F(1,52) = 4.16, p =0.047. There was no difference between participants who practiced and did not practice AT in the five-minute rest period before the video ($M \pm SE = 2.3 \pm 0.7$ vs. 1.7 ± 0.7) but this changed in the first five minutes of the video as soon they began to do AT ($M = 3.8 \pm 0.7$ vs. 1.6 ± 0.8). There were no significant effects in the analyses of HF HRV, SBP, or DBP.

Effects of Applied Tension on Reported Anxiety.

The GLM of pre- and post-experiment State Anxiety scores produced a 4way Condition x Sex x Needle Fear x Time interaction, F(1,59) = 7.22, p = 0.009. To clarify this, separate Condition x Needle Fear analyses of pre-post change in anxiety were conducted for males and females. Consistent with previous results, there were no significant effects among males but a significant Condition x Needle Fear interaction in females, F(1,30) = 6.43, p = 0.017. As can be seen in Figure 3, females with more needle fears who were assigned to the control group reported increased anxiety after viewing the video while higher fear females who practiced AT did not.

Analyses of Covariance.

To examine whether the effect of Applied Tension on vasovagal symptoms was more strongly related to changes in self-reported anxiety or heart rate change, the original GLM of BDRI scores was recalculated using pre-post anxiety change as a covariate. The previous 3-way interaction among Condition, Sex, and Needle Fear was no longer significant (p = 0.15). On the other hand, the interaction remained significant, F(1,57) = 4.81, p = 0.032, when mean heart rate change during the video from the pre-video rest period was substituted for anxiety change as a covariate. In other words, controlling for the impact of AT on anxiety eliminated its effect on vasovagal symptoms. Controlling for the impact of condition on heart rate did not.

Discussion and Introduction to Part Two.

In one respect, the results of Part One are not surprising. That is, the fact that AT benefited primarily people who rated themselves as more fearful of

needles is not surprising since few symptoms would be expected among those who say they are comfortable with needles. On the other hand, the results may provide important directions for future research. First, it was possible to elicit feelings of dizziness and faintness in a laboratory context despite the use of a fairly mild stimulus, at least in comparison to previous studies that used videos of open heart surgery (Steptoe & Wardle, 1988; Vögele et al., 2003). In fact, three participants were sufficiently distressed to the point where it was not possible to obtain physiological recordings. Second, even among the remaining participants who displayed less intense symptoms, an effect of Applied Tension was observed in females who are more fearful of needles. Finally, the results point to the potential importance of anxiety reduction by AT as a mechanism for its effects on vasovagal symptoms. On the other hand, while the pattern of results in Part One is encouraging, one possible limitation concerns the laboratory nature of the investigation. Even though participants were not selected for the presence of needle fears and were probably fairly representative of college students in that regard, it is possible that the results may not be reflective of young adult blood donors who seem even more removed from the idea of blood and injury phobia.

As a result, a preliminary evaluation of this idea was conducted using archival data from a previous clinical trial of AT (Ditto & France, 2006; Ditto, France, et al., 2003). The Medical Fears Survey was included in the donor information questionnaire packet but has not been analyzed until now. The purpose of this analysis was to see if the previously observed impact of Applied Tension on BDRI scores in females (Ditto, France, et al., 2003) was moderated by Needle Fear score.

Method.

Participants.

1,254 volunteer donors at mobile Héma Quebec blood donation clinics held in Montreal-area colleges and universities were tested. 601 males, 653 females were tested, ranging in age from 18-40 years (M = 21.9, SD = 21.9). Participants were pre-screened for blood donor eligibility (Figure 4). Further exclusion criteria included more than five previous blood donations. Participation was voluntary and no payment was provided. The research was approved by the McGill and Héma-Québec IRBs.

Procedure.

After recruitment, participants were assigned randomly, in blocks of 10, to either a group that learned AT using the previously described instructional video and was asked to practice it for the entire time they were on the donation chair, a group that learned AT but was asked to practice it only before the needle was inserted, or a group that did not learn AT and underwent the typical blood donation procedure. Although a number of additional dependent measures were assessed such as whether or not treatment was required to treat a vasovagal reaction, this analysis will focus on BDRI administered while the donor rested afterwards in the refreshment area. For present purposes, the BDRI was re-scored using the current "short" scoring system as in Part One (France et al., 2008). On the other hand, the Medical Fear Survey was administered to only approximately one-half (680) of participants due to the lack of a validated French version (Figure 4). Further information about the sample and procedures can be found in Ditto et al. (Ditto, France, et al., 2003) and Ditto and France (Ditto & France, 2006).

Results.

The primary analysis was a 3 Condition (no Applied Tension/Applied Tension before needle/Applied Tension during donation) x 2 Sex (male/female) x Needle Fear Score GLM. Similar to the laboratory study, despite the use of volunteer blood donors who would not be expected to include people who are especially afraid of needles, a strong main effect of Needle Fear was observed, F(1,653) = 32.46, p < 0.001. People who were more afraid of needles reported significantly more symptoms of dizziness, etc. However, there was also a significant Sex x Condition x Needle Fear interaction, F(2,653) = 3.95, p = 0.020. As can be seen in Figure 5, the pattern of means was similar to the laboratory results. Females with higher needle fears who practiced AT – in this case during an actual blood donation – reported significantly fewer symptoms of dizziness, etc. compared to similar females who did not practice AT. The benefit of AT was limited mostly to people who reported higher levels of needle fear.

Discussion

The version of AT used to date in blood clinics involving repeated 5-s cycles of isometric muscle tension is somewhat less intense than the classic clinical version used with blood phobics involving longer 10-20-s periods of tension (Ost et al., 1991). The briefer cycle is used to better match a procedure often used by phlebotomists that is, having the donor "pump" the muscles in the arm with the donation needle to speed blood flow and reduce donation time. Regardless, though the idea of longer cycles is worth further examination, the exercise involved in AT was sufficient to raise heart rate. AT involves repeatedly tensing all of the major muscle groups in the body and the 5-s cycle has been

found to increase heart rate and blood pressure in people who are not exposed to blood and injury stimuli (France et al., 2006). In principle, it might have been expected that the increase in heart rate would have been associated with a decrease in parasympathetic, vagal activity and, as a result, high frequency heart rate variability (Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996) but this was not the case. If anything, the present results suggest that the increase in heart rate was the result of a cardiac sympathetic activity. Further research is required to clarify the physiological effects of AT and how they interact with the vasovagal process. At the same time, it seems as though the effects of AT on vasovagal symptoms cannot be attributed entirely to exercise-related cardiovascular activity.

Consistent through the results is the idea that individuals with more medical fears experienced more stress and vasovagal symptoms. This was reflected in both self-report (vasovagal symptoms, anxiety) and physiological measures. For example, people with more medical fears displayed increasing skin conductance before the venipuncture video. In general, this applied to both males and females and is not surprising as individuals who are blood and injury phobic experience higher levels of anxiety and stress when exposed to blood donation related cues (Page, 1994), though both the intensity of fear and the Part One stimulus were less strong than previous research.

Despite this, Applied Tension was useful in reducing self-reported vasovagal symptoms such as dizziness, lightheadedness, and weakness though in this case the findings are limited to females who are more fearful about needles. The fact that AT reduced symptoms in females more than males despite equal

changes in exercise-related heart rate, as well as the fact that AT reduced anxiety in females but not males supports the idea that AT's effects on vasovagal symptoms are at least partially mediated by anxiety reduction. They are also consistent with suggestions that AT works better in reducing clinical blood donation-related symptoms in females (Ditto, France, et al., 2003). But why do females experience more anxiety reduction with AT than males? It is possible that females have higher beliefs that this technique will be effective. We have previously found that females were more likely than males to say that they would recommend muscle tensing to a friend who was going to give blood (Ditto, France, et al., 2003). Alternatively, the sex difference may spring from greater scepticism among males or a tendency to attribute positive blood donation experience to one's own intrinsic resilience rather than a technique.

As noted above, Applied Tension was originally developed as an adjunct to exposure therapy for blood and injury phobias. However, it soon became apparent that the tension component may, in and of itself, be useful not just to reduce fear-related fainting but fear. For example, Öst and colleagues (Ost et al., 1991) had three groups of blood and injury phobics who either 1) learned how to practice repeated muscle tension and were exposed to blood and injury stimuli, 2) were repeatedly exposed to blood and injury stimuli, or 3) learned the muscle tensing technique but were given explicit "anti-exposure" instructions during treatment, that is, that they should not expose themselves to blood and injury stimuli. Regardless of whether it was combined with exposure or not, people who learned muscle tension displayed similar general and specific improvements, e.g., ability to watch a video depicting surgery. The authors suggest that learning the

coping technique may reduce anxiety about the possibility of encountering such stimuli. A subsequent study by this group (Hellström, Fellenius, & Öst, 1996) found that one session of tension training could produce positive effects for phobics, consistent with the present application in blood donors.

Medical care often involves stressful and invasive procedures that elicit anxiety and, at times, fainting. While this typically involves needles (Ditto & Holly, 2009), sharp objects are not always involved. For example, vasovagal reactions occur occasionally during colonoscopy (Neri et al., 2007) and even purely non-invasive scans can elicit considerable anxiety and worry about fainting (Thorpe, Salkovskis, & Dittner, 2008). Complications can range from outright faints to premature termination of the procedure to avoidance of the procedure altogether. Applied Tension may be useful in a number of health-related contexts.
Figure 1: Results of a General Linear Model on Vasovagal Symptoms



Figure 1. Vasovagal symptom scores (+ *SE*) in relation to condition, sex, and needle fear. Error bars represent standard errors. For illustrative purposes, needle fear is displayed as a median split (low/high fear). Higher fear individuals reported significantly more vasovagal symptoms than those with low fear and this was reduced in females using AT.

Figure 2: Results of a General Linear Model of Interbeat Intervals



Figure 2. Interbeat interval values before the venipuncture video during Section One intervals by condition. Interbeat interval remained stable in the control condition and decreased (heart rate increased) in AT group. Error bars represent standard errors.

Figure 3: Results of General Linear Model of Pre-Post State Anxiety Scores



Figure 3. Pre-post experiment anxiety change in females (by condition and needle fear). This figure indicates an increase in anxiety over the course of the experiment in higher fear females who did not practice AT. This increase was eliminated with the practice of AT.

Figure 4: Sampling and Flow of Subjects Through a Randomized Trial in Part

Two



Figure 4. Participant flow in Part Two following Consolidated Standards of Reporting Trials guidelines. MFS = Medical Fears Survey. AT = Applied Tension.

Figure 5: Results of a General Linear Model on Vasovagal



Figure 5. Vasovagal symptom scores in relation to condition and sex in Part Two. Females with higher needle fear who practiced AT during blood donation experienced fewer vasovagal symptoms compared to similar females who did not practice AT. Error bars represent standard error.

Acknowledgements

This research was supported by grants from the Canadian Blood Services and the Canadian Institutes of Health Research.

References

- Ditto, B., Byrne, N., & Holly, C. D. (2009). Physiological correlates of applied tension may contribute to reduced fainting during medical procedures. *Annals of Behavioral Medicine*, *37*(3), 306-314.
 doi: 10.1007/s12160-009-9114-7
- Ditto, B., & France, C. R. (2006). The effects of applied tension on symptoms in French-speaking blood donors: a randomized trial. *Health Psychology*, 25(3), 433-437. doi: 10.1037/0278-6133.25.3.433
- Ditto, B., France, C. R., Albert, M., & Byrne, N. (2007). Dismantling applied tension: mechanisms of a treatment to reduce blood donation-related symptoms. *Transfusion*, 47(12), 2217-2222.
 doi: 10.1111/j.1537-2995.2007.01449.x
- Ditto, B., France, C. R., Lavoie, P., Roussos, M., & Adler, P. S. (2003). Reducing reactions to blood donation with applied muscle tension: a randomized controlled trial. *Transfusion*, 43(9), 1269-1275.
 doi: 10.1111/j.1537-2995.2007.01449.x
- Ditto, B., & Holly, C. D. (2009). Emotional Stress, Dizziness, and Fainting. In A. Lindqvist & G. Nyman (Eds.), *Dizziness: Vertigo, Disequilibrium and Lightheadedness* (pp. 83-99): Nova Science Publishers Inc.
- Ditto, B., Wilkins, J. A., France, C. R., Lavoie, P., & Adler, P. S. (2003). On-site training in applied muscle tension to reduce vasovagal reactions to blood donation. *Journal of Behavioral Medicine*, 26(1), 53-65.
 doi: 10.1023/A:1021795022380

Task Force of the European Society of Cardiology and the North American
Society of Pacing Electrophysiology, (1996). Heart Rate Variability :
Standards of Measurement, Physiological Interpretation, and Clinical Use. *Circulation*, 93(5), 1043-1065. doi: 10.1161/01.CIR.93.5.1043

Foulds, J., Wiedmann, K., Patterson, J., & Brooks, N. (1990). The effects of muscle tension on cerebral circulation in blood-phobic and non-phobic subjects. *Behaviour Research and Therapy*, 28(6), 481-486. doi: 10.1016/0005-7967(90)90134-5

- France, C. R., Ditto, B., France, J. L., & Himawan, L. K. (2008). Psychometric properties of the Blood Donation Reactions Inventory: a subjective measure of presyncopal reactions to blood donation. *Transfusion*, 48(9), 1820-1826. doi: 10.1111/j.1537-2995.2008.01831.x
- France, C. R., France, J. L., & Patterson, S. M. (2006). Blood pressure and cerebral oxygenation responses to skeletal muscle tension: a comparison of two physical maneuvers to prevent vasovagal reactions. *Clinical Physiology and Functional Imaging*, 26(1), 21-25.
 doi: 10.016/j.transci.2003.08.014
- France, C. R., France, J. L., Roussos, M., & Ditto, B. (2004). Mild reactions to blood donation predict a decreased likelihood of donor return. *Transfusion* and Apheresis Science, 30(1), 17-22. doi: 10.1016/j.transci.2003.08.014
- Gillespie, T. W., & Hillyer, C. D. (2002). Blood donors and factors impacting the blood donation decision. *Transfusion Medicine Reviews*, 16(2), 115-130. doi: 10.1053/tmrv.2002.31461

- Hellstrom, K., Fellenius, J., & Öst, L. G. (1996). One versus five sessions of applied tension in the treatment of blood phobia. *Behavior Research and Therapy*, 34(2), 101-112. doi: 0005-7967(95)00060-7
- Hellström, K., Fellenius, J., & Öst, L. G. (1996). One versus five sessions of applied tension in the treatment of blood phobia. *Behaviour Research and Therapy*, 34(2), 101-112. doi: 10.1016/0005-7967(95)00060-7
- Kleinknecht, R. A., Thorndike, R. M., & Walls, M. M. (1996). Factorial dimensions and correlates of blood, injury, injection and related medical fears: Cross validation of the Medical Fear Survey. *Behaviour Research and Therapy*, 34(4), 323-331. doi: 10.1016/0005-7957/(95)00072-0
- Meade, M. A., France, C. R., & Peterson, L. M. (1996). Predicting vasovagal reactions in volunteer blood donors. *Journal of Psychosomatic Research*, 40(5), 495-501. doi: 10.1016/0022-3999(95)00639-7
- Neri, E., Caramella, D., Vannozzi, F., Turini, F., Cerri, F., & Bartolozzi, C.
 (2007). Vasovagal reactions in CT colonography. *Abdominal Imaging*, 32(5), 552-555. doi: 10.1007/s00261-006-9055-6
- Ost, L. G., Fellenius, J., & Sterner, U. (1991). Applied tension, exposure in vivo, and tension-only in the treatment of blood phobia. *Behavior Research and Therapy*, 29(6), 561-574. doi: 0005-7967(91)90006-O
- Ost, L. G., & Sterner, U. (1987). Applied tension. A specific behavioral method for treatment of blood phobia. *Behavior Research and Therapy*, 25(1), 25-29. doi: 10.1016/0005-7967(87)90111-2
- Ownby, H. E., Kong, F., Watanabe, K., Tu, Y., & Nass, C. C. (1999). Analysis of donor return behavior. *Transfusion*, *39*(10), 1128-1135.

doi: 10.1046/j.1537-2995.1999.39101128.x

- Page, A. C. (1994). Blood-injury phobia. *Clinical Psychology Review*, *14*(5), 443-461. doi: 10.1016/0272-7358(94)90036-1
- Sarlo, M., Buodo, G., Munafo, M., Stegagno, L., & Palomba, D. (2008).
 Cardiovascular dynamics in blood phobia: evidence for a key role of sympathetic activity in vulnerability to syncope. *Psychophysiology*, 45(6), 1038-1045. doi: 10.1111/j.1469-8986.2008.00713.x
- Spielberger, C. D., Gorsuch, R. L., & Edward, L. R. (1970). STAI manual for the state-trait anxiety inventory ("self-evaluation questionnaire"): Consulting Psychologists Press
- Steptoe, A., & Wardle, J. (1988). Emotional fainting and the psychophysiologic response to blood and injury: autonomic mechanisms and coping strategies. *Psychosomatic Medicine*, 50(4), 402-417.
- Thorpe, S., Salkovskis, P. M., & Dittner, A. (2008). Claustrophobia in MRI: the role of cognitions. *Magnetic Resonance Imaging*, 26(8), 1081-1088. doi: 10.1016/j.mri.2008.01.022
- Vögele, C., Coles, J., Wardle, J., & Steptoe, A. (2003). Psychophysiologic effects of applied tension on the emotional fainting response to blood and injury. *Behaviour Research and Therapy*, *41*(2), 139-155.
 doi: 10.1016/S0005-7967(01)00133-4

TRANSITION

There were several advantages to the research presented in Manuscript One. This includes the blending of laboratory and clinical research and, as a result, internal and external validity. The results of both studies suggest that anxiety is an important moderator of the effects of Applied Tension and that AT may work in part by reducing blood donation-related anxiety. However, the clinical research described in Manuscript One was archival and not designed with anxiety reduction in mind. As a result, another trial of AT was conducted for Manuscript Two focussing on a comparison of the effects of AT applied in the donation chair or while waiting for blood donation.

During a typical blood donation clinic there is a brief to moderate waiting period, e.g., 30-60 minutes. While this is virtually inevitable, given limitations of equipment and staff and the unpredictability of donor turnout, anxiety about the impending blood donation can increase. A foremost recommendation to blood donor clinics in reducing vasovagal symptoms is to reduce the waiting times (Crocco & D'Elia, 2007). Ratings of predonation anxiety have been commonly associated with increased vasovagal symptoms (Ditto & France, 2006; Olatunji, Etzel, & Ciesielski, 2010) Additionally, physiological changes indicative of presyncopal responses such as increases in blood pressure can be noted during this pre-donation period (Adler, Ditto, France, & France, 1994). Given that anxiety is so important in subsequent vasovagal reactions, it seems that it may be too late to begin Applied Tension during the donation, particularly if its effects are not mediated primarily by exercise-related blood pressure maintenance. The standard application is to begin when the needle is inserted in the arm. Only one study has

investigated alternative timing/earlier use of this technique. However, Applied Tension was used only for a two minute interval prior to donation which would not be sufficient to have a significant impact, on either blood pressure or anxiety. In fact, it was viewed as a placebo condition (Ditto, France, Lavoie, Roussos, & Adler, 2003).

Manuscript Two was designed to test the idea of pre-donation AT more explicitly. A 2 pre donation applied Tension (yes/no) by 2 during donation applied Tension (yes/no) design was used to help identify the best timing of AT and shed light on the mechanisms of action. If applied Tension works in part through anxiety reduction, it would seem logical to start the intervention in the early stages of anxiety.

References

Adler, P., Ditto, B., France, C., & France, J. (1994). Cardiovascular reactions to blood donation in offspring of hypertensives and normotensives. *Journal* of Psychosomatic Research, 38(5), 429-439.
doi: 10.1016/0022-3999(94)90104-X

Crocco, A., & D'Elia, D. (2007). Adverse reactions during voluntary donation of blood and/or blood components. A statistical-epidemiological study. *Blood Transfusion*, 5(3), 143-152. doi: 10.2450/2007.0005-07

- Ditto, B., & France, C. R. (2006). Vasovagal symptoms mediate the relationship between predonation anxiety and subsequent blood donation in female volunteers. *Transfusion*, 46(6), 1006-1010. doi: 10.1111/j.1537-2995.2006.00835.x
- Ditto, B., France, C. R., Lavoie, P., Roussos, M., & Adler, P. S. (2003). Reducing reactions to blood donation with applied muscle tension: a randomized controlled trial. *Transfusion*, 43(9), 1269-1275.
 doi: 10.1046/j.1537-2995.2003.00488.x

Olatunji, B. O., Etzel, E. N., & Ciesielski, B. G. (2010). Vasovagal syncope and

blood donor return: examination of the role of experience and affective expectancies. *Behavior Modification*, *34*(2), 164-174. doi: 10.1177/0145445510362576

MANUSCRIPT TWO

APPLIED TENSION AND COPING WITH BLOOD DONATION: A RANDOMIZED TRIAL

Holly, C. D., Torbit, L., Ditto, B. (Online First). Applied Tension and coping withblood donation: a randomized trial. *Annals of Behavioral Medicine*.doi: 10.1007/s12160-011-9315-8

Abstract

Background

Despite the ongoing need for blood donation, few people give blood. A common reason is concern about vasovagal symptoms.

Purpose

The aim of this study was to evaluate the effectiveness of Applied Tension in reducing vasovagal symptoms during blood donation and the mechanisms of action.

Method

Two hundred eighty-two young adult blood donors were randomly assigned to conditions involving Applied Tension during the pre-donation wait period, during the blood draw, both, or no Applied Tension at all.

Results

Applied Tension was effective in reducing vasovagal symptoms in blood donors, particularly when practiced during the pre-donation wait period (p < 0.001). People who practiced Applied Tension during the pre-donation wait period required less treatment for vasovagal reactions than people who did not (8% vs. 16%).

Conclusions

The results of this study suggest that the effects of Applied Tension on vasovagal symptoms are not mediated entirely by exercise-related changes in blood pressure and heart rate. Rather, it may reduce anxiety or physiological consequences of anxiety. Applied Tension is a useful treatment which can help people cope during blood donation and other invasive medical interventions.

Keywords: Applied Tension, Vasovagal syncope, Blood donation, Anxiety Introduction

Despite widespread agreement on the medical and social importance of blood donation, only a small proportion of the population, e.g., approximately 3% in the USA (Gillespie & Hillyer, 2002), gives blood. As pressing as current needs are, this is going to be an even greater problem in the future as the population ages and new uses for blood are developed. At the same time, safety-related concerns have lead to increasing rates of blood donor deferrals and exclusions (Riley, Schwei, & McCullough, 2007). These considerations underscore the importance of ensuring that people who are healthy enough and willing enough to volunteer to give blood become and remain donors. Unfortunately, there are a number of disincentives to giving blood. Perhaps the most important is the fact that blood donation is not always a pleasant experience. Considerable research indicates that the common experience of unpleasant vasovagal symptoms during blood donation significantly reduces the chance of subsequent donation (France, France, Roussos, & Ditto, 2004; Newman, Newman, Ahmad, & Roth, 2006).

Applied Tension is a promising behavioral technique that has been shown to reduce the occurrence of vasovagal symptoms in people undergoing a medical intervention (Ditto, France, Lavoie, Roussos, & Adler, 2003). These symptoms range from light headache and dizziness to full-out fainting (vasovagal syncope). Applied Tension was originally developed by Öst and Sterner for use with blood, injection, and injury phobics (Ost & Sterner, 1987). Compared to the typical fear reaction involving sympathetic activation and an increase in blood pressure, there is often a unique "diphasic" cardiovascular response to feared stimuli in blood,

injection and injury phobics. Initially, the expected increase in heart rate (HR) and blood pressure (BP) are seen, but they are followed swiftly by decreases in HR and BP increasing the risk for vasovagal symptoms due to a decrease in cerebral blood flow (Graham, Kabler, & Lunsford, 1961; Kleinknecht, 1987), though there has been some recent discussion of this model (Ritz, Meuret, & Ayala, 2010). Öst et al. found that repeated isometric muscle tension was a successful intervention for the dizziness and fainting that many of his blood phobic patients experienced while practicing exposure therapy (Hellstrom, Fellenius, & Öst, 1996; Öst, Fellenius, & Sterner, 1991; Öst & Sterner, 1987) as it presumably maintained HR and BP.

While research shows that Applied Tension can reduce vasovagal symptoms, the mechanisms by which it works are not entirely clear. The exercise-related component of Applied Tension maintains HR and BP in blood, injection and injury phobics exposed relevant stimuli (Vögele, Coles, Wardle, & Steptoe, 2003) and blood donors while giving blood (Ditto, Byrne, & Holly, 2009), but it is not clear if this is responsible for symptom reductions. For example, in the context of a laboratory investigation of Applied Tension, we recently observed significant general increases in HR and BP just before participants watched a video depicting blood draws, but Applied Tension reduced symptoms only among female participants (Holly, Balegh, & Ditto, 2011). Similarly, Ditto and colleagues (Ditto, France, et al., 2003) found that female blood donors who practiced Applied Tension reported fewer symptoms and required less treatment for vasovagal symptoms as compared to a no-treatment and a placebo group, but males did not experience these benefits. This suggests

that other factors besides exercise-related change in HR and BP are responsible for the impact on symptoms, perhaps involving anxiety reduction.

Despite its origin as a treatment for blood, injection and injury phobia, the possible anxiety-reducing aspects of Applied Tension have not been emphasized in relation to its effects on blood donation. This is probably due to the fact that blood donors are obviously not blood, injection and injury phobics. Indeed, as a group, they are likely less fearful of blood, injection and injury stimuli than the general population. On the other hand, while a voluntary activity, it is wellknown that people decide to give blood for a variety of reasons ranging from a general social benevolence, concern about a natural or manmade disaster such as 9/11 (Glynn et al., 2002), a sense of personal debt after a loved one receives a transfusion, or even friendly coercion (Sojka & Sojka, 2008). As a result, all donors are not necessarily at ease with needles and the donation procedure in general. A number of investigators have noted an increase in anxiety before donation (Ditto & France, 2006; Gillespie & Hillyer, 2002), and Meade and colleagues (Meade, France, & Peterson, 1996) found that fear-related psychological variables were better predictors of vasovagal symptoms in this environment than more commonly used demographic predictors such as age, sex, and previous blood donation experience. This may be related to the fact that donation usually involves a significant wait before giving blood. The typical process involves reading informative material, registration, and a blood and health screen even before waiting for the next available donation chair. While attempts are made to expedite the procedure in order to prevent discouraging donors (McKeever, Sweeney, & Staines, 2006), only so much can done to reduce the

potentially stressful wait. Interestingly, Hanson and France (Hanson & France, 2009) found that extra social support by volunteers during waiting reduced vasovagal symptoms.

In sum, it is possible that psychological aspects of Applied Tension such as distraction and providing a coping behaviour reduce donor anxiety and are responsible for some of the effects on vasovagal symptoms (Ditto, France, Albert, & Byrne, 2007; Ditto, France, et al., 2003). That is, Applied Tension may dampen both the first as well as the second stage of the diphasic response. If this is the case, donors might benefit from Applied Tension during the waiting period as well as during the actual procedure as typically done. In one previous study (Ditto, France, et al., 2003), we administered Applied Tension during the waiting period but only for a very brief period (approximately 2 minutes) very late in the wait period. The present study sought to examine the effects of Applied Tension by looking at its impact on blood donation-related anxiety, physiological activity, and vasovagal symptoms and more thoroughly study the impact of the timing of Applied Tension on these measures. It was predicted that Applied Tension would reduce both anxiety and vasovagal symptoms and that practicing Applied Tension before as well as during blood donation would reduce these measures.

Method

Participants and Experimental Conditions.

Participants (maximum age = 40 years) were recruited at mobile blood clinics held by the provincial blood collection agency, Héma-Québec between 2008 and 2009. People were recruited and assigned randomly (through a randomly generated number list) to experimental condition upon entry. When approached, participants had previously been screened for basic eligibility to donate blood and but not been through the medical screening interview nor had participated in any other activities. Written informed consent was obtained from all participants. They were assigned to one condition in a 2 x 2 design, that is, whether or not they would practice Applied Tension during the pre-donation wait period and whether or not they would practice Applied Tension while giving blood (Figure 6). As all participants were donating blood, they were subsequently screened for medical issues and exclusionary criteria for blood donation, ensuring a group of healthy young adults. Consistent with the random assignment of participants to conditions, there were no significant differences in demographic variables (Table 1) though one–age–approached significance, F(3, 280) = 2.52, p= 0.058. As a result, age was included as a covariate in all analyses. All participants were English speaking. The study was approved by the relevant ethical human subjects committees of McGill University and Héma-Québec.

Apparatus.

Physiological measurements were obtained at the beginning and end of the blood donation procedure. Systolic (SBP) and diastolic blood pressure (DBP, in millimetres of mercury) and heart rate (HR, in beats per minute) were obtained using a Datascope Accutorr Plus blood pressure monitor (www.datascope.com). Participants learned AT by watching a 2-min instructional video used in previous research (Ditto, France, Albert, Byrne, & Smyth-Laporte, 2009) on a notebook computer. The video depicts repeated 5-s on, 5-s off cycles of whole body isometric while maintaining regular breathing. Participants were asked to tense the muscles of their legs, abdomen, and arms at 5-s intervals at a level comparable

to "squeezing a tennis ball." They were also told to breathe normally and not hold their breath while tensing. Inadvertent viewing of the video (by control subjects or non-participants) was not possible.

Questionnaires.

Participants completed a number of questionnaires before and after blood donation. Prior to donation, participants completed a short demographic questionnaire and the Spielberger State Anxiety Inventory (Spielberger, Gorsuch, & Edward, 1970). The Spielberger State Anxiety Inventory is a 20-item selfreport scale where various mood statements are rated on a five-point Likert scale ranging from 1 (not at all) to 4 (very much). After donation, while sitting in the recovery area, participants completed a longer questionnaire including the Spielberger State Anxiety Inventory and the Blood Donation Reactions Inventory (Meade et al., 1996). The Blood Donation Reactions Inventory is a wellvalidated, self-report index of 11 vasovagal symptoms such as dizziness, lightheadedness, and nausea. Items are rated on a six-point Likert scale ranging from 0 (not at all) to 5(to an extreme degree). They rated the pain of the predonation screening fingerprick and donation needle insertion on 165mm visual analog scales with legends of no pain and extreme pain. Finally, participants also completed a general measure of medical fears, the Medical Fears Survey (Kleinknecht, Thorndike, & Walls, 1996) (not discussed in the present report), as well as a treatment evaluation questionnaire inquiring about treatment compliance and acceptance.

Procedure and Research Assistant Measures.

After recruitment, participants completed the brief (to minimize interference with the blood donation procedure) pre-donation questionnaire and measurements of BP and HR were obtained. Those assigned to an Applied Tension group were taught the technique via the instructional video. Participants in a before-donation Applied Tension group were instructed to begin practicing Applied Tension from that moment on, until they arrived at the blood donation chair. Those in a during-donation group were instructed to practice Applied Tension from the moment they got on the donation chair until they were just about to get up. Participants in the combined group were asked to practice throughout the entire process. Research assistants monitored participants in the clinic and reminded them to comply with their Applied Tension directives. All continued through the standard blood donation procedure.

During blood donation, a research assistant visited each participant at bedside and recorded information such as a rating from the nurse of the difficulty of needle insertion, the participant's compliance with Applied Tension directives, whether or not the participant fainted, and whether or not treatment was required for a vasovagal reaction. Treatment for a reaction included reclining the donor's chair and occasionally placing a damp cloth on the forehead. After the participant sat on the donation chair but before needle insertion the research assistant also asked them to rate how relaxed they felt on a 0 (not relaxed at all)-100 (fully relaxed) scale. This question was repeated just before the participant was about to get off the donation chair. Donors were not questioned directly about vasovagal symptoms while in the donation chair to minimize interference with the collection process and the possibility of inadvertently increasing the chance of a reaction.

However, they completed the Blood Donation Reactions Inventory and other components of the post-donation questionnaire immediately afterward in the postdonation recovery area while consuming a snack. Another set of physiological measures was obtained after the questionnaire was completed.

Data Analyses and Reduction.

Mean values of BP and HR were calculated before and after donation. Pre- to post-donation change scores were computed for BP and HR. A recent factor analysis of Blood Donation Reactions Inventory items (France, Ditto, France, & Himawan, 2008) revealed four items (dizziness, faintness, weakness, and lightheadedness) that reflect the primary vasovagal experience. As a result, ratings of these items were summed and, consistent with previous research, logtransformed to reduce skewness. Similarly, pre- and post-donation Spielberger State Anxiety Inventory scores and the other behavioral measures were logtransformed. Preliminary analyses revealed no significant interactions between the effects of condition and sex, primarily main effects of sex on baseline (predonation) values of the physiological measures. As a result, the primary analyses were 2 Applied Tension Pre-donation (yes, no) x 2 Applied Tension During Donation (yes, no) analyses of covariance (ANCOVAs) using age as a covariate. The analyses of physiological change scores included the initial baseline values as another covariate. All analyses were conducted on an intent-to-treat basis.

Results

Self-Report Anxiety.

Spielberger State Anxiety Inventory scores were analyzed using a 2 Applied Tension Pre-donation x 2 Applied Tension Pre-donation x 2 Time (pre-

donation questionnaire, post-donation questionnaire) ANCOVA. A strong effect of Time was observed, F(1,253) = 28.38, p < 0.001, indicating that participants felt more anxious before than after donation but no other significant effects were observed. However, these observations (just after recruitment and sitting in the post-donation recovery area) may have been too far removed from treatment to reveal an effect. Consistent with this idea, the 2 Applied Tension Pre-donation x 2 Applied Tension during donation x 2 Time (just before needle insertion, just before leaving donation chair) ANCOVA of participants ratings of in-chair relaxation produced a significant Applied Tension Pre x Applied Tension During interaction, F(1,275) = 3.95, p = 0.048. A one-tailed t-test was conducted to compare anxiety levels between those who did and did not practice Applied Tension as it was predicted that participants in Applied Tension conditions would experience less anxiety than participants in the no-treatment control condition. As can be seen in Figure 7, participants asked to practice Applied Tension pre- but not during donation said they were more relaxed than those who did not practice Applied Tension, t(136) = -1.87, p = 0.032. Participants in the other Applied Tension groups reported being somewhat, but not significantly, more relaxed than no-treatment participants.

Treatment Compliance.

Since the research assistants only rated compliance while the participant was in the donation chair, which did not include the pre-donation wait period, the main indicator was whether or not the participant said they used the assigned technique. Ninety-four percent of participants said they used their assigned

technique on the post-donation questionnaire. There were no differences between groups.

Pain and Vasovagal Symptoms.

There were no significant effects of treatment on fainting though consistent with previous research outright faints were rare (only 11 participants fainted). However, the ANCOVA of Blood Donation Reactions Inventory scores revealed a significant main effect of practicing Applied Tension Pre-donation, F(1, 274) = 4.52, p = 0.034, as well as a significant Applied Tension Pre x Applied Tension During Interaction, F(1, 274) = 14.01, p < 0.001. As can be seen in Figure 8, participants who practiced Applied Tension before but not during donation as well as participants who practiced Applied Tension during but not pre donation reported significantly fewer vasovagal symptoms than no-treatment participants, t(134) = 4.08, p < 0.001 and t(140) = 2.12, p = 0.018, respectively. There were no significant effects in the analyses of pain ratings, suggesting relatively specific effects of treatment on vasovagal symptoms. Consistent with this, a logistic regression of nurse-initiated treatment for vasovagal symptoms revealed a significant main effect of practicing Applied Tension before arriving at the donation chair, odds ratio (OR) = 0.46, 95% confidence interval (CI) = 0.21 -0.97, p = 0.042. Overall, people who practiced Applied Tension before they got to the donation chair were less likely to require treatment (chair reclining) compared to those who did not (8% vs. 16%).

Finally, pairwise comparisons of the participant's rating of how strongly they would recommend muscle tensing to a friend who was going to give blood in the three groups who practiced some form of Applied Tension (before, during, or

both, pairwise comparisons were necessary since people who did not practice Applied Tension did not rate this variable) revealed that there was no difference between people who practiced Applied Tension either before or during donation, but people in both of these groups were more enthusiastic about Applied Tension than participants who were asked to practice Applied Tension from the very beginning to the very end, t(133) = 1.89, p = 0.031 and t(123) = 1.83, p = 0.035.

Physiological Data.

No significant group differences (or anything approaching significance) were found in any of the baseline physiological measurements (Table 1). There were no significant effects of practicing Applied Tension, either before or during donation, on change in systolic blood pressure or heart rate. However, the main effect of Applied Tension during was significant in the ANCOVA of diastolic blood pressure change, F(1,265) = 4.04, p = 0.045. In general, people who did not practice Applied Tension while in the donation chair had no change in DBP (X = -0.5 ± 0.7 mmHg) while those who practiced Applied Tension in the chair had a significant increase in DBP (X = 1.6 ± 0.7 mmHg).

Discussion

This study used a modified version of Öst's traditional "clinical version" of Applied Tension - cycling in 5-s intervals versus 10-20-s intervals of Tension (Ost et al., 1991). The 5-s cycling better matches the demands placed on blood donors by the phlebotomists when asked to pump their arm muscles in order to speed the blood donation. While the overall rate of fainting (vasovagal syncope) in participants was low, vasovagal symptoms were nevertheless common. Twelve percent of blood donors required some form of treatment during the donation and

71 % reported experiencing at least one mild vasovagal symptom during donation such as dizziness and nausea on the Blood Donation Reactions Inventory.

The clearest impact of Applied Tension was among those who practiced it before arriving at the chair though it is interesting to note that for those who were not asked to do Applied Tension in this early stage of the donation process, participants who practiced Applied Tension while they were actually in the chair reported fewer symptoms than participants who did not (Figure 7). In this respect, the results replicate previous findings of the effects of Applied Tension (Ditto, France, et al., 2003; Ditto, Wilkins, France, Lavoie, & Adler, 2003). However, the clearest benefit, including a reduction in nurse-initiated treatment for vasovagal symptoms, came from practicing Applied Tension before arriving at the chair. Confidence in this effect is enhanced by the fact that the nurses who conducted the blood draws did not interact with donors until they arrived at the chair and thus were blind to whether or not the participant was using Applied Tension earlier. This finding supports the belief that while the exercise-related cardiovascular effects of Applied Tension may play some role in reducing symptoms, they cannot explain the full impact of Applied Tension.

Although participants may have been anxious before arriving at the chair and needle insertion, blood pressure does not start to drop until the blood draw begins. If the only benefit comes from exercise-related maintenance of heart rate and blood pressure, practicing Applied Tension before arriving at the chair is much too soon.

Applied Tension appears to work at least in part by some kind of stressbuffering mechanism, either reducing anxiety or perhaps the physiological

consequences of anxiety. That said, the results may appear inconsistent with a previous study (Ditto, France, et al., 2003) in which we found that a brief predonation period of Applied Tension did *not* reduce symptoms. However, Applied Tension was administered for a very limited amount of time (2 min) late in the wait period (just before needle insertion). As a result, it was more properly considered a placebo intervention since participants were lead to believe it might be effective but there was insufficient time for it to have a significant psychological or physiological effect. Thus, Applied Tension does not appear to be simply a placebo, producing its effects by the expectation of positive benefit, though the exact stress-buffering effects remain to be determined. These may include distraction, social support, and respiratory control. Distraction has been found to improve coping with invasive medical procedures such as dentistry (Furman et al., 2009), injections, and chemotherapy (McCarthy et al., 2010; Schneider, Kisby, & Flint, 2011). Similarly, in another study of blood donors (Ditto et al., 2007), we found that asking some participants to pay particular attention to the arm that did not have the needle in it while just tensing their arms (presumably to develop a better sense of the amount of muscle tension) decreased symptoms more than no treatment though not as well as full body Applied Tension.

Social support has also been implicated as an important factor in the blood donation process. In a recent study, Hanson and France (Hanson & France, 2009) found that donors who were accompanied by a research assistant who provided encouragement and engaged in small talk experienced fewer reactions. While participants in the present study who practiced Applied Tension during the wait

period were not accompanied by a research assistant, it is possible that they felt less isolated being part of the "team" that was testing Applied Tension, especially compared to the no-treatment control participants who underwent the normal blood collection procedure.

Finally, it is also possible that practicing during the stressful wait period had a beneficial effect in terms of maintaining regular breathing. While participants were not asked to breathe in concert with the 5-s cycles of muscle tension, it is likely that many did since it is a comfortable pace and the video encouraged people to breathe regularly, albeit to discourage breath-holding. Ritz and colleagues (2010) recently suggested that emotional fainting is due less to a diphasic cardiovascular response than altered breathing patterns that lead to hypocapnia. The idea that anxiety-driven changes in respiratory activity may be responsible for many vasovagal symptoms is consistent with observations such as the much higher rates of reactions among young and inexperienced donors (Byrne & Ditto, 2005; Labus, France, & Taylor, 2000), associations between anxiety and blood donation reactions (Olatunji, Etzel, & Ciesielski, 2010), and, in the present case, the apparent importance of pre-donation intervention. Even though Applied Tension was not conceived as a means to regularize breathing, it is possible it affects are mediated by effects on respiration as much as cardiovascular activity.

There were several limitations to the research. For example, the study environment did not permit continuous measurement of BP and HR which may have limited the ability to detect intervention-related cardiovascular changes. Similarly, it was not possible to collect electromyographic measures that would have allowed better assessment of compliance with muscle-tensing instructions.

Given the coaching involved in learning Applied Tension, the public nature of blood clinics, and participant self-reports, it seems likely that compliance was reasonable. However, further research is required to determine whether outcome varies with treatment compliance. Analyses were conducted on an intention-totreat basis which may provide a conservative estimation of the treatment effect due to non-compliance; however, this was deemed the most appropriate approach as it most closely represents the real clinical situation (Heritier, Gebski, & Keech, 2003). Finally, another interesting puzzle is why participants who were asked to practice Applied Tension throughout the pre-donation and donation process did not seem to benefit quite as much (though not significantly less) from Applied Tension as those in the pre-donation only condition. A speculative explanation, partially supported by ratings of how much they would recommend Applied Tension to a friend, is that this request was viewed as too demanding, and as a result, these participants practiced Applied Tension with less enthusiasm. In any case, practicing Applied Tension while waiting for the procedure to begin seems particularly helpful.

Applied Tension is a useful treatment for both phobic and non-phobic individuals undergoing blood donation. The mechanisms of treatment in these two situations may not be identical but seem closer than originally anticipated and do not appear limited to exercise-induced changes in cardiovascular activity. Applied Tension is a simple, practical intervention that may help people cope better with a variety of invasive medical procedures.

	No AT pre- donation		AT pre-donation	
	No AT	AT during	No AT	AT during
	during	donation	during	donation
	donation		donation	
Ν	70	75	67	70
Sex (% female)	43 (61.4%)	40 (53.3%)	32 47.7%	51.4%
Age	20.8 (3.2)	20.7 (3.3)	19.7 (1.8)	21.1 (3.5)
BMI	22.7 (3.2)	22.7 (3.3)	23.6 (4.0)	23.2 (4.1)
Baseline SBP (mmHg)	119.1 (1.6)	118.8 (1.6)	119.8 (1.5)	118.0
				(1.5)
Baseline DBP (mmHg)	71.5 (1.1)	71.7 (1.1)	72.5 (1.1)	71.2 (1.1)
Baseline HR (bpm)	79.4 (1.4)	77.7 (1.4)	77.2 (1.4)	76.8 (1.4)
Donation experience	1.8 (2.8)	2.0 (2.6)	1.6 (1.6)	2.0 (2.4)
(previous donations)				
Needle insertion	1.6 (0.9)	1.6(0.9)	1.5 (0.7)	1.6 (0.9)
difficulty (nurse's 1-5				
rating)				

Table 1. Demographic characteristics of participants.





Figure 6. Participant flow chart following Consolidated Standards of Reporting

Trials Guidelines. AT = Applied Tension.

Figure 7: Results of 2 Way ANOVA on Relaxation Scores.



Figure 7. Effect of practicing AT pre- and/or during donation (Condition) on inchair ratings of relaxation (log units). AT = Applied Tension. Error bards represent standard error.

Figure 8: Results of an ANCOVA on Vasovagal Symptoms.



Figure 8. Effect of practicing AT pre and/or during donation on vasovagal symptoms measured by the Blood Donations Reaction Inventory (BDRI log units). AT = Applied Tension. Error bars indicate standard error.

Conflict of Interest Statement: The authors of this research have no conflicts of interest to disclose.

Acknowledgments

This research was supported by grants from the Canadian Institutes of Health Research and the Canadian Blood Society. The assistance of Héma Québec is gratefully acknowledged.
References

Byrne, N., & Ditto, B. (2005). Alexithymia, cardiovascular reactivity, and symptom reporting during blood donation. *Psychosomatic Medicine*, 67(3), 471-475. doi: 10.1097/01.psy.0000160471.66399.12

Ditto, B., Byrne, N., & Holly, C. D. (2009). Physiological correlates of applied tension may contribute to reduced fainting during medical procedures.
 Annals of Behavioral Medicine, *37*(3), 306-314.
 doi: 10.1007/s12160-009-9114-7

- Ditto, B., & France, C. R. (2006). Vasovagal symptoms mediate the relationship between predonation anxiety and subsequent blood donation in female volunteers. *Transfusion*, 46(6), 1006-1010.
 doi: 10.1111/j.1537-2995.2006.00835.x
- Ditto, B., France, C. R., Albert, M., & Byrne, N. (2007). Dismantling applied tension: mechanisms of a treatment to reduce blood donation-related symptoms. *Transfusion*, 47(12), 2217-2222.
 doi: 10.1111/j.1537-2995.2007.01449.x

Ditto, B., France, C. R., Albert, M., Byrne, N., & Smyth-Laporte, J. (2009).
Effects of applied muscle tension on the likelihood of blood donor return. *Transfusion*, 49(5), 858-862. doi : 10.1111/j.1537-2995.2008.02067.x

Ditto, B., France, C. R., Lavoie, P., Roussos, M., & Adler, P. S. (2003). Reducing reactions to blood donation with applied muscle tension: a randomized controlled trial. *Transfusion*, 43(9), 1269-1275.
doi: 10.1111/j.1537-2995.2007.01449.x

Ditto, B., Wilkins, J. A., France, C. R., Lavoie, P., & Adler, P. S. (2003). On-site training in applied muscle tension to reduce vasovagal reactions to blood donation. *Journal of Behavioral Medicine*, *26*(1), 53-65.
doi: 10.1023/A:1021795022380

France, C. R., Ditto, B., France, J. L., & Himawan, L. K. (2008). Psychometric properties of the Blood Donation Reactions Inventory: a subjective measure of presyncopal reactions to blood donation. *Transfusion*, 48(9), 1820-1826. doi: 10.1111/j.1537-2995.2008.01831

- France, C. R., France, J. L., Roussos, M., & Ditto, B. (2004). Mild reactions to blood donation predict a decreased likelihood of donor return. *Transfusion* and Apheresis Science, 30(1), 17-22. doi: 10.1016/j.transci.2003.08.014
- Furman, E., Jasinevicius, T. R., Bissada, N. F., Victoroff, K. Z., Skillicorn, R., & Buchner, M. (2009). Virtual reality distraction for pain control during periodontal scaling and root planing procedures. *The Journal of the American Dental Association, 140*(12), 1508-1516.
- Gillespie, T. W., & Hillyer, C. D. (2002). Blood donors and factors impacting the blood donation decision. *Transfusion Medicine Reviews*, 16(2), 115-130. doi: 10.1053/tmrv.2002.31461

Glynn, S. A., Kleinman, S. H., Schreiber, G. B., Zuck, T. F., Mc Combs, S., Bethel, J., et al. (2002). Motivations to donate blood: demographic comparisons. *Transfusion*, 42(2), 216-225.
doi: 10.1046/j.1537-2995.2002.00008.x

Graham, D. T., Kabler, J. D., & Lunsford, L. J. (1961). Vasovagal fainting: A diphasic response. *Psychosomatic Medicine*, *23*(6), 493-507.

- Hanson, S. A., & France, C. R. (2009). Social support attenuates presyncopal reactions to blood donation. *Transfusion*, 49(5), 843-850.doi: 10.1111/j.1537-2995.2008.02057.x
- Hellstrom, K., Fellenius, J., & Öst, L. G. (1996). One versus five sessions of applied tension in the treatment of blood phobia. *Behavior Research and Therapy*, 34(2), 101-112. doi: 0005-7967(95)00060-7
- Heritier, S. R., Gebski, V. J., & Keech, A. C. (2003). Inclusion of patients in clinical trial analysis: The intention-to-treat principle. *The Medical Journal of Australia*, 179, 438-440.
- Holly, C. D., Balegh, S., & Ditto, B. (2011). Applied tension and blood donation symptoms: the importance of anxiety reduction. *Health Psychology*, *30*(3), 320-325. doi: 10.1037/a0022998
- Kleinknecht, R. A. (1987). Vasovagal syncope and blood/injury fear. *Behavior Research and Therapy*, 25(3), 175-178. doi: 0005-7967(87)90043-X
- Kleinknecht, R. A., Thorndike, R. M., & Walls, M. M. (1996). Factorial dimensions and correlates of blood, injury, injection and related medical fears: Cross validation of the Medical Fear Survey. *Behaviour Research and Therapy*, 34(4), 323-331. doi: 10.1016/0005-7967(95)00072-0

Labus, J., France, C., & Taylor, B. (2000). Vasovagal reactions in volunteer blood donors: Analyzing the predictive power of the medical fears survey. *International Journal of Behavioral Medicine*, 7(1), 62-72. doi: 10.1207/s15327558ijbm0701_5

McCarthy, A. M., Kleiber, C., Hanrahan, K., Zimmerman, M. B., Westhus, N., & Allen, S. (2010). Factors explaining children's responses to intravenous

needle insertions. Nursing Research, 59(6), 407-416. doi:

410.1097/NNR.1090b1013e3181f1080ed1095.

- McKeever, T., Sweeney, M. R., & Staines, A. (2006). An investigation of the impact of prolonged waiting times on blood donors in Ireland. *Vox Sanguinis*, 90(2), 113-118. doi: 10.1111/j.1423-0410.2006.00734.x
- Meade, M. A., France, C. R., & Peterson, L. M. (1996). Predicting vasovagal reactions in volunteer blood donors. *Journal of Psychosomatic Research*, 40(5), 495-501. doi: 10.1016/0022-3999(95)00639-7
- Newman, B. H., Newman, D. T., Ahmad, R., & Roth, A. J. (2006). The effect of whole-blood donor aderse events on blood donation return rates. *Transfusion*, 46(8), 1374-1379. doi: 10.1111/j.1537-2995.2006.00905.x
- Olatunji, B. O., Etzel, E. N., & Ciesielski, B. G. (2010). Vasovagal syncope and blood donor return: examination of the role of experience and affective expectancies. *Behavior Modification*, *34*(2), 164-174. doi: 10.1177/0145445510362576
- Ost, L. G., Fellenius, J., & Sterner, U. (1991). Applied tension, exposure in vivo, and tension-only in the treatment of blood phobia. *Behavior Research and Therapy*, 29(6), 561-574. doi: 0005-7967(91)90006-O
- Ost, L. G., & Sterner, U. (1987). Applied tension. A specific behavioral method for treatment of blood phobia. *Behavior Research and Therapy*, 25(1), 25-29. doi: 10.1016/0005-7967(87)90111-2
- Riley, W., Schwei, M., & McCullough, J. (2007). The United States' potential blood donor pool: estimating the prevalence of donor-exclusion factors on the pool of potential donors. *Transfusion*, 47(7), 1180-1188.

doi: 10.1111/j.1537-2995.2007.01252.x

- Ritz, T., Meuret, A. E., & Ayala, E. S. (2010). The psychophysiology of bloodinjection-injury phobia: looking beyond the diphasic response paradigm. *International Journal of Psychophysiology*, 78(1), 50-67. doi: 10.1016/j.ijpsycho.2010.05.007
- Schneider, S., Kisby, C., & Flint, E. (2011). Effect of virtual reality on time perception in patients receiving chemotherapy. *Supportive Care in Cancer*, 19(4), 555-564. doi: 10.1007/s00520-010-0852-7
- Sojka, B. N., & Sojka, P. (2008). The blood donation experience: self-reported motives and obstacles for donating blood. *Vox Sanguinis*, 94(1), 56-63. doi: 10.1111/j.1423-0410.2007.00990.x
- Spielberger, C. D., Gorsuch, R. L., & Edward, L. R. (1970). STAI manual for the state-trait anxiety inventory ("self-evaluation questionnaire"): Consulting Psychologists Press.
- Vögele, C., Coles, J., Wardle, J., & Steptoe, A. (2003). Psychophysiologic effects of Applied Tension on the emotional fainting response to blood and injury. *Behaviour Research and Therapy*, *41*(2), 139-155. doi: 10.1016/S0005-7967(01)00133-4

GENERAL DISCUSSION

The research presented in this thesis aimed to contribute to the literature on the relationship between anxiety and vasovagal symptoms and the effectiveness of Applied Tension in reducing these symptoms. Specifically, these studies examined Applied Tension as a treatment for vasovagal reactions in the context of blood donation and the role anxiety plays in vasovagal reactions. Moreover, this set of studies was designed to acquire both physiological data through a laboratory setting (Manuscript One) and to investigate in an ecologically valid clinical setting (the blood donor clinic), (Manuscripts One and Two). Overall findings support the notion that AT is effective in reducing vasovagal symptoms and that anxiety reduction is as important, if not more important than simple exercise-related increases in cardiovascular activity. Relatively consistent with previous research, these findings also suggest that AT is not equally effective for all individuals. Notably, females showed greater reductions in vasovagal symptoms when using AT than males, as did individuals with higher levels of needle fears.

Manuscript One investigated the physiological and psychological mechanisms involved in vasovagal responses to a laboratory stimulus and found an interesting pattern of results supporting the notion that anxiety is involved in the effectiveness of Applied Tension on vasovagal symptoms. This relationship indicated that AT does not work simply by moderating heart rate and blood pressure. To further delineate the mechanisms through which AT works, Manuscript Two investigated the utility of AT prior to and / or during blood donation and found that the most effective timing was prior to blood donation. It

is not uncommon to have a considerable wait period (e.g., 30 minutes) for a blood donation. Manuscript Two showed that AT is effective by reducing anxiety, which may in fact increase during this period.

All the same, these findings do not explain why a muscle tensing technique can reduce anxiety. While it is important to understand that psychological processes contribute to the effectiveness of this technique, it begs the question of how repeated muscle tension effects anxiety. There are several possible connections. Applied Tension was conceived originally as an adjunct to exposure therapy in treating individuals with blood phobia by Öst and Sterner (1987). Somewhat ironically, since it was designed as a physiological approach to induce arousal (at least increased heart rate and blood pressure), it emerged serendipitously as a treatment to reduce fainting. However, it strongly resembles the commonly practiced treatment, progressive muscle relaxation (PMR), used in treating anxiety. Through tensing and subsequently releasing muscles, PMR induces a sensation of relaxation which can counter or lower anxiety. The main differences between AT and PMR lie in the nature of the muscle tension (AT involves tensing both the upper and lower body muscles all at once, not one after the other) and the fact that with AT the focus is on the tension as compared to PMR where the focus is on relaxing. Thus, blood donors who practice AT are not typically told to focus on pleasant sensation associated with releasing muscle tension. Regardless, a pleasant "massaging" sensation may contribute to decreased anxiety with AT.

When the effects of AT are explored in this framework, another similarity with classic relaxation strategies comes to light: rhythmic activity. In AT and

PMR there is a focus on maintaining a steady and appropriate rhythm of the activity and breath. Many common stress reduction strategies employ a rhythmic approach such as tai chi, meditation using a repetitive mantra, even listening to music. In all these approaches rhythmic practice is encouraged while other thoughts of possibly obsessive or unpleasant stimuli are directed to more relaxing thoughts or focus on the repetitive stimuli. Even mindfulness, an emerging trend in health psychology which involves acknowledgement and non-avoidance of distressing thoughts, employs repetitiveness. While practicing mindfulness present attentional focus is encouraged, including strong awareness of repetitive breathing.

The possibility that AT may regularize breathing is an especially interesting idea for future research given research on anxiety-related overbreathing. It may also explain the "paradoxical" anxiety-related decrease in arousal that characterizes vasovagal syncope. From noticeable deep breathing to marked hyperventilation, numerous researchers have documented the role of overbreathing in both vasovagal syncope and blood, injection and injury phobias (Ayala, Meuret, & Ritz, 2010; Foulds, Wiedmann, Patterson, & Brooks, 1990; Steptoe & Wardle, 1988). Strong associations have also been found between respiratory dysregulation and hyperventilation and disgust (Ayala et al., 2010), a potentially important factor in fainting though it is unclear if irregular breathing patterns are a result or a cause of anxiety (Roth, 2005). Nonetheless, a core principle of anxiety treatment is teaching regular breathing and the appropriate rate and this provides a reduction of anxiety symptoms. When practicing Applied Tension, participants are instructed: "breathe normally" and "don't hold your

breath while tensing or release in a gush when you stop. Just keep breathing normally". While individuals practicing AT were not trained to breathe in any particular manner it may be that their focus was turned to their respiration and the instructions are sufficient to influence and stabilize breathing to some degree. This may contribute to a reduction in anxiety and risk for vasovagal symptoms. Ritz and colleagues (2010) have recently argued that vasovagal symptoms may not be due to a diphasic cardiovascular response. Rather, they suggest that hyperventilation, primarily through increased tidal volume, may be the key component in syncope. Ritz (2010) notes that overbreathing leads to vasodilation in the periphery which may cause pooling of blood and cerebral vasoconstriction that reduces cerebral perfusion, both of which could increase the chances of fainting. Hence, this may be an important factor in understanding the syncopal response and the effectiveness of AT.

Finally, another explanation for the reduction in anxiety with AT may be simple attentional focusing. It may be that practicing Applied Tension redirects one's focus to a distracting activity and away from an anxiety producing situation. Distraction has long been used in medical interventions. By providing a method of attentional focus away from the anxiety producing stimuli and onto something else (in this case practicing Applied Tension), anxiety may be reduced. Indeed, previous research (Ditto, France, Albert, & Byrne, 2007) supports the notion that Applied Tension provides a distracting activity and that at least part of AT's effect springs from distraction. However, distraction is not an effective method of coping for everyone. Bonk and colleagues found reduced blood donation

reactions in those that prefer and employed distraction as a coping technique during a blood donation (Bonk, France, & Taylor, 2001).

Another interesting area for future research concerns the paradoxical nature of the vasovagal response. As discussed previously, the decrease in arousal associated with vasovagal syncope is puzzling in a number of respects. What are its mechanisms? Ritz's suggestion of anxiety and respiratory-related hypocapnia is an interesting idea though that still leaves open the issue of the origin of this response. Is vasovagal syncope a "biological accident"? Perhaps, although many have argued strongly that it is not (e.g., Alboni, Brignole, Degli & Uberti, 2007; Bracha, 2004; Diehl, 2005). For example, Alboni and colleagues (2007) argue that vasovagal syncope is not a "disease" in part by noting that the lifetime prevalence of vasovagal syncope in the general population is close to 50% and the neural processes involved are probably universal in healthy humans. What might have led to the development of this response? A speculative but interesting idea is proposed by Bracha and colleagues (e.g., Bracha, 2004; Bracha, Bracha, Williams, Ralston, & Matsukawa, 2005) who suggest that fainting as a result of exposure to needles or other instruments is the result of an evolutionary response to modern weapons that are designed to pierce and cut. They suggest the response developed since people who fainted were more likely to survive an attack of an overwhelming opponent, causing the aggressor to believe that they were successful and turn their attention to other activities/potential victims. Similar versions of this theory have been used to explain animals who feign death.

A comparable, perhaps more plausible evolutionarily driven hypothesis, was suggested by Diehl (2005). Fainting is not due solely to the peripheral

hemodynamic effects of blood loss but an active, central mechanism which temporarily shuts down the organism. This response may be adaptive to reduce blood loss and facilitate repair by clotting. It is well established that once blood loss begins to exceed 30% blood volume there is active suppression of sympathetic and enhancement of parasympathetic activity (Schadt & Ludbrook, 1991), which is not so different than what happens with emotional fainting. Perhaps this evolutionarily driven response is stimulated when facing what is perceived as a stressful situation involving potential blood loss.

Future research should further investigate the role of anxiety in vasovagal reactions and anxiety reduction in Applied Tension. The future of blood donation is constantly growing. Children are now permitted to engage in autologous or directed donations prior to surgery or other medical treatments that may require blood. Given that children experience vasovagal reactions as frequently or more frequently than adults and that donations are typically ceased if such reactions occur, it is important to take measures to reduce their occurrence. Additionally, reactions are common in children during routine vaccination or immunization clinics. In any of these situations a simple technique could be easily taught and applied to reduce potential negative symptoms without disrupting the process; Applied Tension could provide a developmentally appropriate technique for use with children experiencing vasovagal symptoms.

Individuals who experience vasovagal symptoms or syncope have difficulties which span well beyond the blood donation clinic; visits to the dentist, simple blood draws and minor medical procedures can all induce vasovagal symptoms. Treatments to address these reactions may be helpful, cost effective

and easy to implement across varied medical environments. Applied Tension is a plausible, affordable treatment of syncope and further studies into its anxiety reducing properties will enhance the applicability of this technique.

References

- Alboni, P., Brignole, M., Delgi Uberti, E. C. (2007). Is vasovagal syncope a disease ? *Europace 9*(2), 83-87. doi: 10.1093/europace/eul179
- Ayala, E. S., Meuret, A. E., & Ritz, T. (2010). Confrontation with blood and disgust stimuli precipitates respiratory dysregulation in blood–injection–injury phobia. *Biological Psychology*, 84(1), 88-97.
 doi: 10.1016/j.biopsycho.2010.02.004
- Bonk, V. A., France, C. R., & Taylor, B. K. (2001). Distraction reduces selfreported physiological reactions to blood donation in novice donors with a blunting coping style. *Psychosomatic Medicine*, 63(3), 447-452.
- Bracha, H. S. (2004). Freeze, flight, fight, fright, faint; Adaptationist perspectives on the acute stress response spectrum. *CNS Spectrums*, *9*(9), 679-685.
- Bracha, H. S., Bracha, A. S., Williams, A. E., Ralston, T. C., & Matsukawa, J. M. (2005). The human fear-circuitry and fear-induced fainting in healthy individuals. *Clinical Autonomic Research*, *15*(3), 238-241.
 doi: 10.1007/s10286-005-0245-z
- Diehl, R. (2005). Vasovagal syncope and Darwinian fitness. *Clinical Autonomic Research*, 15(2), 126-129. doi: 10.1007/s10286-005-0244-0

Ditto, B., France, C. R., Albert, M., & Byrne, N. (2007). Dismantling applied tension: mechanisms of a treatment to reduce blood donation-related symptoms. *Transfusion*, 47(12), 2217-2222.
doi: 10.1111/j.1537-2995.2007.01449.x

- Foulds, J., Wiedmann, K., Patterson, J., & Brooks, N. (1990). The effects of muscle tension on cerebral circulation in blood-phobic and non-phobic subjects. *Behaviour Research and Therapy*, 28(6), 481-486. doi: 10.1016/0005-7967(90)90134-5
- Öst, L. G., & Sterner, U. (1987). Applied tension. A specific behavioral method for treatment of blood phobia. *Behavior Research and Therapy*, 25(1), 25-29. doi: 10.1016/0005-7967(87)90111-2
- Ritz, T., Meuret, A. E., & Ayala, E. S. (2010). The psychophysiology of bloodinjection-injury phobia: looking beyond the diphasic response paradigm. *International Journal of Psychophysiology*, 78(1), 50-67. doi: 10.1016/j.ijpsycho.2010.05.007
- Roth, W. T. (2005). Physiological markers for anxiety: Panic disorder and phobias. *International Journal of Psychophysiology*, 58(1-2), 190-198. doi: 10.1016/j.ijpsycho.2005.01.015
- Schadt, J. C., & Ludbrook, J. (1991). Hemodynamic and neurohumoral responses to acute hypovolemia in conscious mammals. *Heart*, 260(2), 305-318.
- Steptoe, A., & Wardle, J. (1988). Emotional fainting and the psychophysiologic response to blood and injury: autonomic mechanisms and coping strategies. *Psychosomatic Medicine*, 50(4), 402-417.