Utility of an Animated Bowel Biofeedback Training Routine to Improve Bowel Function in Individuals With SCI

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STUDY TITLE: Utility of an Animated Bowel Biofeedback Training Routine to Improve Bowel Function in Individuals with SCI

A. SPECIFIC AIMS

Biofeedback techniques are known to decrease the frequency of fecal incontinence (FI) in able-bodied (AB) populations and improve reflex defection in persons who experience constipation. We hypothesize that bowel biofeedback training in spinal cord injured (SCI) patients will result in the following:

In subjects with decreased external sphincter strength and control (FI subjects): Improved objective bowel function parameters as measured by anorectal manometry, a decrease of FI episodes, a decrease in Wexner's incontinency score and a decrease in the SCI Bowel Surveys Score.
In subjects with tonic, constricted external sphincter and missing/decreased recto-anal inhibitory reflex (RAIR) (constipation subjects): An increase in sensitivity and strength of the RAIR and decreased symptoms of constipation (Bowel and Bladder Survey).

Specific Aims:

1. To assess baseline motility characteristics (resting pressure, squeezing pressure, high pressure zone, and RAIR) in persons with chronic SCI.
   We hypothesize that individuals with SCI will have abnormal resting pressures (either increased or decreased, decreased squeezing pressures and an impaired RAIR reflex.

2. To determine the characteristics of SCI (level, completeness, baseline manometric parameters) which best predict the outcome of the biofeedback training. Additionally, we aim to assess the efficacy of bowel biofeedback therapy in SCI patients in improving:

   a) Changes in maximum rectal and sphincter pressures generated during "squeeze" and "bear down" maneuvers performed during anorectal manometric studies pre-post treatment.
      We hypothesize that due to the learning and conditioning effects of the biofeedback training, we will observe increases in generated sphincter pressures.
   b) Changes to the sensitivity and strength of response of the RAIR reflex in response to rectal distension.
      We hypothesize that the RAIR response will may be partially restored or strengthened by biofeedback training.
   c) FI and constipation as assessed by the Bowel Surveys and Wexner's Incontinence Scale.
      We hypothesize that biofeedback will improve subjective symptoms of FI, constipation, or both.

B. BRIEF REVIEW OF RESULTS OF OTHERS AND CURRENT STAGE OF KNOWLEDGE

SCI results in a multiplicity of secondary medical complications, including neurogenic bowel. Neurogenic bowel as a sequela of SCI, is characterized by difficulty with evacuation (DWE), chronic abdominal pain and fecal incontinence (FI). There are approximately 300,000 individuals with SCI in the United States. SCI affects 12,700 new patients every year in the USA

and this number is projected to increase to 17,560 in 2050 [1]. The incidence of SCI is lower (10,000 new patients per year) in the European Union. Studies have shown variable incidence of FI in SCI patients; the incidence of FI in these studies ranged from 15% to 85% depending on completeness of the spinal lesion. Valles *et al*. conducted a study in 54 patients with motor complete SCI and reported the following; constipation in 67% of patients and FI in 85% of patients [2]. In a self report survey study of 424 SCI individuals, Krogh *et al*. reported fecal incontinence in 75% of SCI patients at least once per year, 20% at least once per month and 5% once per day [3]. It is clear that bowel dysfunction is a common and distressing problem in these individuals, and it significantly affects the quality of life of SCI patients [4]. Studies assessing the influence of bowel function on quality of life have showed, that up to 65% patients with SCI had quality of life issues compared to 8% of AB patients [5].

Neurogenic bowel characteristics differ among SCI individuals, and appear to depend primarily on the level and completeness of injury. It is thought that upper motor neuron lesions in the spinal cord above the conus medullaris (L1-2) results in a hyperreflexive bowel with increased colonic wall tone and loss of cortical control over the relaxation of the external anal sphincter (EAS). These changes result in chronic high sphincter tone and dyssynergic defecation. The main symptoms in these patients are constipation and fecal retention, or difficulty with evacuation (DWE). In many of these individuals, some nerve connections between the spinal cord and the colon may be preserved, and stool propulsion and reflex coordination may remain intact and under control of the central nervous system [3, 6]. Furthermore, individuals with spinal lesions above T7 experience loss of voluntary control over abdominal muscles and an inability to increase intra-abdominal pressure, which results in more DWE and constipation [2]. Lower motor neuron (LMN) lesions in the spinal cord below L1-2 result in the interruption of the centrally mediated innervation to the bowel, which causes slowing of peristalsis, a flaccid EAS, and atonic levator ani muscles. This is also called an areflexic bowel. The main symptoms in these patients are constipation from slowed peristalsis and FI from atonic EAS and levator ani muscles. While the symptoms of bowel dysfunction in persons with SCI are known, function and motility of the anal canal have not been documented in this population. Various techniques, such as the measurement of pressure profiles facilitate assessment of GI motor function. Anorectal manometry can provide valuable information about sphincter strength, defecation dynamics and reflex mechanisms. In the past few decades, motility studies have been conducted using water-perfused systems. These systems consist of a multilumen catheter which is connected to an array of pressure tranducers, a pnuemohydraulic pump to provide the continuous flow of water, and a display system. The pnuemohydraulic pump drives water through very narrow channels of the catheter at a constant low rate, but under very high pressure. Each channel of the catheter is connected to a separate pressure tranducer. Any interference with the flow of water from any of the various channels by lumen occluding contractions in the channel raises pressures in that channel. Pressure transducers continuously monitor pressures in the channels. This information is transmitted to a computer and displayed as line tracings. While useful, such systems are limited by the number of channels each catheter can accommodate as catheter size is limited. This greatly reduces the amount of information that can be captured, especially in small, activity-laden areas such as sphincteric regions. New high-resolution anorectal manometric systems (Given Imaging, Duluth, GA), simultaneously captures pressure data from the rectum, IAS, EAS and atmosphere. These systems allow for tight spacing of many pressure sensors, which allow visualization of short as well as long segment retrograde and anterograde contractions. Short segment retrograde contractions cannot be normally visualized using traditional manometry due

to wide spacing between channels. High resolution manometry also allows for much clearer display of pressure events compared to line tracing series, and direction of contractions are much easier to discern. To date, anorectal high resolution topographical studies have not been conducted in a SCI population.

The aim of most treatment strategies for neurogenic bowel in this population is to regularize bowel movements and preempt constipation. Most often, multifaceted programs (using non- pharmacological and pharmacological methods) are required for the management of neurogenic bowel. The non-pharmacological options include dietary fiber and fluid intake, digital rectal stimulation, and abdominal massage. The pharmacological treatment include use of irritant suppositories and prokinetics. Additional approaches include use of assistive devices like standing tables and modified toilet seats, irrigation techniques and implantation of electrical stimulation devices. Colostomy and implanted irrigation catheters are tried as a last resort. However, these programs are successful in only approximately 67% of patients [3]. There still remain a significant proportion of patients in whom the multifaceted programs are not effective. These patients are burdened by cumbersome and time consuming bowel care programs, recurrent episodes of FI and other secondary complications such as chronic pain and autonomic dysreflexia. Additionally, most standard treatment protocols address the problem of difficulty with evacuation/constipation. While this may be partially effective in preventing overflow incontinence, it does not address the issue of FI that occurs as a result of atonic musculature, or from urgency caused by hypersensitive rectum. Furthermore, these typed of treatment methods are aimed to promote bowel movement without voluntary input from the patient and are not aimed at improving bowel function.

Modalities in which the patient can be trained to control the IAS and EAS are promising solutions to FI, and have been shown to be useful in AB populations [7-9]. For example, anorectal biofeedback methods teach patients to recognize sensations of a distended rectum while also teaching abdominal or pelvic muscles to voluntarily contract for short periods of time in order to improve continence. Such biofeedback modalities have also been shown to decrease constipation in AB populations [10-13] by teaching proper external sphincter relaxation and rectal muscle contraction. The concept of biofeedback is based on principles of operant conditioning, in which information concerning a normally subconscious physiological function in relayed to patients and that become actively engaged in learning to consciously control this function. During bowel (re)training programs, patients are provided with visual feedback on voluntary and reflex sphincter and rectal muscle contractions, so that they can learn to recognize diffuse sensations and gradually regain control.

It may be appreciated that using biofeedback therapy to control the bowel would require presence of some sensation in SCI patients; i.e., motor incomplete SCI patients with partially preserved motor and sensory function. Individuals with SCI are categorized as motor complete or incomplete using the American Spinal Injury Association (ASIA) criteria. Motor complete SCI patients have a higher incidence of FI, attributed to complete loss of motor and sensory feedback to the CNS from the peripheral organs/muscles [4]. However, some patients with motor complete SCI as defined by ASIA criteria, occasionally reported diffuse visceral sensations preceding involuntary colonic mass movement and defecation [14]. Enck *et al*. evaluated fifteen patients with complete SCI using anorectal manometry, and five out of fifteen patients reported some sensation and three out of fifteen reported pain during rectal distension [14]. Therefore, it is reasonable to postulate that some individuals with complete SCI may still benefit from such therapy, arguing for the widespread utility of biofeedback training.

For our pilot study, we are proposing the use of a 12 week biofeedback training to improve anorectal motility and voluntary control of the IAS, EAS and rectal musculature. It is unknown as to what level and completeness of SCI patients can expect to benefit from such treatment. As such, we are planning on enrolling all non-ambulatory SCI subjects with complete or incomplete injuries (ASIA A, B, C or D). Subjects will be enrolled only if they currently report problems with either constipation or FI on a based on survey responses (Ten Item SCI Bowel Survey (10 SCIB) and Wexner's Incontinency Scale (WIS). Anorectal motility pre to post biofeedback training will be performed. We aim to describe the anorectal pressure profile in persons with SCI and to identify responders to biofeedback training. We believe anorectal function will differ according to the level and completeness of injury. Additionally, we seek to define the levels and completeness of injury, and baseline manometric parameters which are predictors of treatment success.

C. PROCEDURES, METHODS AND EXPERIMENTAL DESIGN

This is a prospective, non-randomized, single center clinical trial. SCI patients will be stratified to 4 different arms according to the level of SCI:

- Upper motor neuron (UMN) incomplete (C5-T12)
- Lower motor neuron incomplete (LMN) (L2-S5)
- UMN complete (C5-T12)
- LMN motor neuron complete (L2-S5)

The Inclusion/Exclusion criteria are as follows:

Inclusion Criteria:

- Chronic SCI (duration over 1 year),
- Able-bodied (non-SCI)
- Between the ages of 18-75.

Exclusion Criteria:

- Contraindication to bowel biofeedback,
- Currently pregnant or trying to become pregnant,
- Inability to provide informed consent.

Study Population

Veterans from the JJPVAMC with chronic SCI, who are seen routinely in outpatient clinic and who complain of fecal incontinence or constipation (Screening Questionnaire: Appendix 1). Additional healthy AB veterans and/or non-veterans will be included in the study population as controls.

Recruitment and Enrollment:

We propose to recruit and enroll patients with SCI who suffer from FI. Patients with SCI who are followed by an SCI primary care physician at the James J Peters Veterans Affairs Medical Center (JJP VAMC) are from a large geographical area (New York, New Jersey, Connecticut, and Pennsylvania) and are referred to this Center for treatment and management of their chronic SCI. Veterans are evaluated in the SCI Clinic where a primary care physician, a registered nurse and a medical assistant evaluate, assess and treat the patients for routine medical care, preventive medicine and urgent care. In FY 2005-2006, 165 unique SCI patients had a total of 295 inpatient stays at the JJP VAMC. In fiscal year 2007, 900 patient encounters were recorded from the SCI

outpatient clinic (stop code 210), of which 200 were unique patients and 182 annual physical exams (mean=15 per month). On average, the SCI Clinic has been successful at recruiting 10 subjects per month for other studies, suggesting our goal of recruiting 50 patients during the 12-month study period is feasible. Patients who visit the SCI clinic for a routine examination will be provided information regarding study participation by their primary care physician. If the patient is interested in study participation, a research coordinator will review the study procedures with the subject, and informed consent will be signed and a medical history questionnaire will be administered. Additionally, both SCI and AB subjects will be recruited if they indicated interest in being contacted for other studies during participation in a previous center research study.

Part 1: Anorectal Manometry:
For Part 1 of the study (Anorectal Manometry), 50 SCI subjects will be stratified into the following groups:

- Group 1: UMN complete,
- Group 2: UMN incomplete,
- Group 3: LMN complete and
- Group 4: LMN incomplete injury.

Fifty subjects will first undergo an SCI ASIA Impairment examination performed by a trained SCI research staff member. Upon completion of the ASIA exam to determine completeness/incompleteness of the injury, all subjects will undergo an anorectal manometry and a baseline assessment of level of constipation or frequency of FI. Approximately 15 AB subjects will also undergo anorectal manometry and serve as a comparison group for baseline measures. The 10 Question Bowel Survey, and Wexner's Incontinence Scale (Appendix 2) will be administered to both groups. All SCI subjects will also complete 3 additional surveys: SCI Bowel Management QOL, SCI Bladder Complication, and SCI Bladder Management. These surveys will test the sensitivity of the SCI-QOL measures within the context of existing interventional studies by comparing it with the legacy tool(s) being used. All manometry studies for AB and SCI subjects will be scheduled for bowel care days (post bowel care routine) to decrease the incidence of incidental bowel movement. After informed consent has been obtained, all subjects will be asked to arrive on the morning of the scheduled visit to the SCI Research Unit (Suite 7A-13). Subjects will be transferred onto a commode bed and asked to lie on their left side. A sheathed and lubricated probe with an inflatable balloon attached to the distal end, will be inserted into the rectum. The probe will be outfitted with an EMG sensor in order to monitor pelvic floor muscle activity. The manometric study will last for approximately 45 minutes and will consist of the following tests, during which muscle activity and pressure will be monitored.

1. Baseline assessment- after a period of acclimation, subjects will be asked to relax for a 30 second period, in which they will be asked to refrain from performing any squeezing or bearing down maneuvers.
2. Squeezing maneuvers- subjects will be asked to squeeze their sphincter muscles as if they were retaining stool. Squeezing maneuvers will be performed until 3 consistent attempts are made.
3. Bearing down maneuvers- subjects will be asked to bear down as though they were attempting to move their bowels. Bearing down maneuvers will be performed until 3 consistent attempts are made.
4. Assessment of the rectoanal inhibitory reflex (RAIR)- a balloon distension test will be performed. The rectal balloon attached to the pressure probe will be gradually filled with air starting at 30ccs and in 10cc increments until a RAIR reflex is identified. Balloon distension increases pressure registered by intrarectal sensors. The volume of air injected is displayed along with the pressure change it induced. Balloon distension normally produces a graded relaxation of the anal canal musculature. The RAIR reflex should appear as a relaxation of the IAS which starts on the rectal side of the anal canal which spreads caudally.

Manometric Parameters

RESTING	SQUEEZE
Maximum sphincter pressure	Maximum sphincter pressure

Mean sphincter pressure Length of IAS and EAS Length of anal verge to centre of anal canal <u>BEAR DOWN</u> Residual anal pressure Percentage anal relaxation Intrarectal pressure Rectoanal pressure differential	Duration of sustained squeeze <u>BALLOON INFLATION (cc)</u> Presence of rectoanal inhibitory reflex (RAIR) First sensation Urge to defecate Discomfort Minimum rectal compliance Maximum rectal compliance

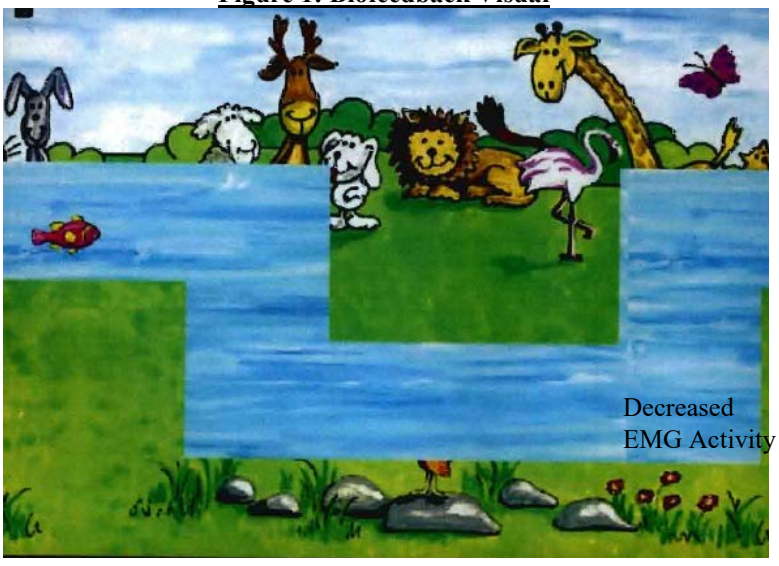
The 10 Question Bowel Survey, SCI Bowel Management QOL, SCI Bladder Complication, SCI Bladder Management, and Wexner's Incontinence Scale will be administered. A subgroup of 20 subjects who report either constipation or FI and who have an incomplete injury as defined by the ASIA Impairment Scale will be identified, and will have the option of enrolling in part 2 of the study; standard bowel biofeedback training.

Part 2: Biofeedback Training:

Once a subject has been identified as a candidate for biofeedback based on the ASIA examination (SCI incomplete ASIA B, C, D) and expressed interest in participation, an informed consent interview will be scheduled. Once written consent is obtained, a training schedule of twice weekly sessions will be scheduled. Twenty subjects will be recruited for this arm of the study. Each training session will last for approximately 60 minutes.

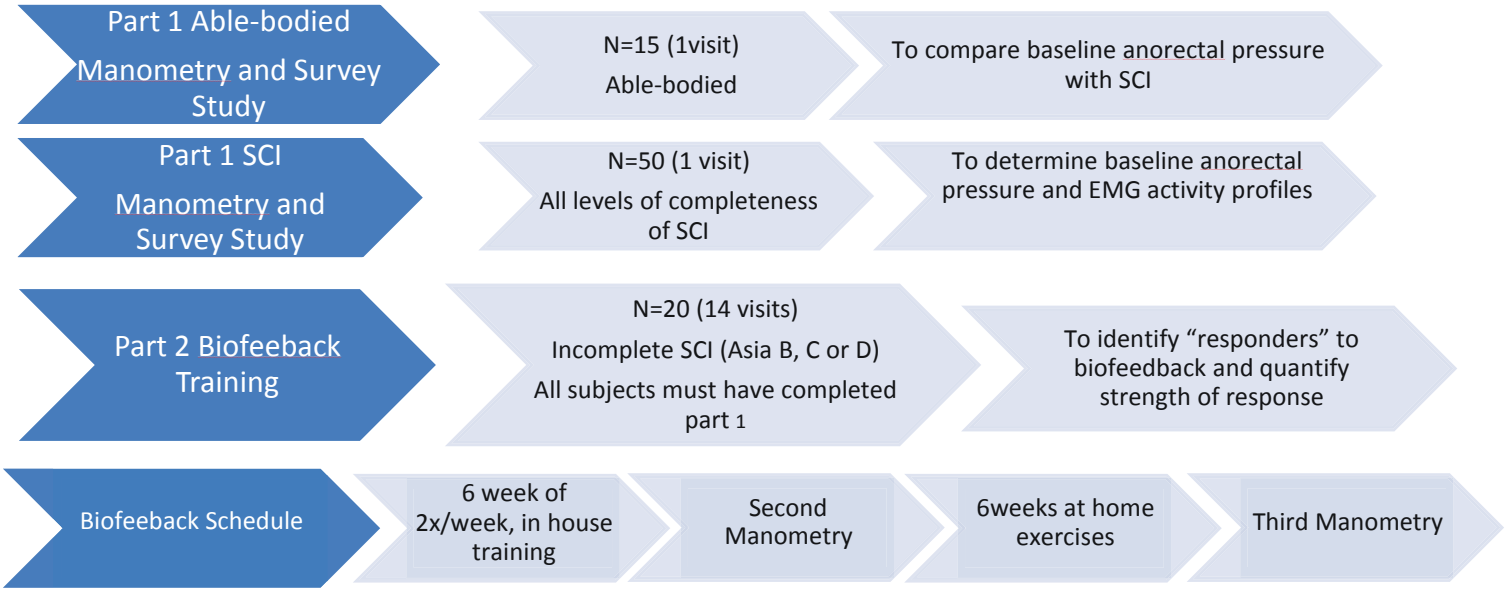
All training session will take place at the SCI Research Unit (Suite 7A-13). Subjects will be transferred onto a commode bed and asked to lie on their left side. A small disposable electromyography (EMG) plug electrode will be inserted into the rectal cavity, which will permit the subject to watch the trace of pelvic floor muscle activity (Figure 1) at rest, during voluntary contraction (squeeze) and during relaxation (bearing down). The subject will be asked to try to follow the visual prompts for approximately 30 minutes; for example, in the visual provided in Figure 1, the subject will be asked to try to guide the fish through the stream by voluntarily contracting and relaxing their pelvic floor muscles. These tracings will increase in levels of difficulty and complexity, as the subject is able accurately (< 10 percent error) reproduce the tracing in the level, within set times. Response to balloon distension will be performed following the tracing exercises. The EMG

Figure 1: Biofeedback Visual



probe will be removed, and a pressure probe with EMG sensor will be inserted. An inflatable balloon will be at the distal end of each probe. The balloon will be distended to until an urge to defecate occurs or to a maximum of 150 ccs. The subject will be asked try and retain the balloon by squeezing the pelvic muscles. Based on each individual subject's baseline abilities, between 5- 50 squeezes will be attempted/performed during the first sessions. Repetitions and target pressures will be increased from session to session based on individual gains. No more than 15 minutes will be spent on balloon distension trials. These sessions will be performed twice a week for 6 weeks. After 6 weeks of in-house training, each subject will undergo another manometric and survey study identical to Part 1 of the study. Subsequently, each subject will be sent home with a personalized training schedule, and will be asked to perform repetitions of squeezing and bearing down maneuvers two times a week. Each typical at home exercise program should last 30 minutes. After 6 weeks of home exercises, a third manometric study will be performed, and bowel surveys will be administered.

Study Timeline



We are proposing three year study duration.

Years 1 and 2: 25 SCI subjects for anorectal manometry; 5 AB subjects; and 10 incomplete SCI subjects for biofeedback training (per year).
Year 3: Results dissemination.

D. PREVIOUS WORK DONE BY YOU OR YOUR COLLABORATORS ON THIS OR RELATED PROJECTS, LISTING PUBLICATIONS

We have been studying the effects of SCI on the bowel functions and management of these patients for the past ten years. Our initial data suggests that there is slowing of intestinal peristaltic activity, likely due to down regulation of parasympathetic neural pathways. To the best of our knowledge there are no studies in the literature addressing the efficacy of biofeedback training on fecal continence in SCI patients. In addition bowel function parameters have not been well defined using high resolution anorectal manometry in SCI patients. We believe that we will be the first to use this new modality to assess anorectal functions and integrate its utility in biofeedback treatment in SCI patients.

Published Work

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E. SIGNIFICANCE OF THIS RESEARCH

The VA cares for approximately 40,000 veterans with SCI. In addition there are over 200,000 non-veterans with SCI in the US. Many of these individuals have neurogenic bowel and suffer from the embarrassment and social isolation caused by FI. The life expectancy of SCI patients has dramatically increased, with most SCI patients living up to 60 years of age (10 years less than non SCI patients). Given that the average age of injury is 37 years and that 25% of SCI patients are between 19 to 25 years, these individuals have to live with the ignominy of fecal incontinence for many years to come. The current practice of using multifaceted programs for bowel care leaves much to be desired, as many SCI patients still suffer from FI and constipation. In this respect it has become urgent to develop other treatment options for neurogenic bowel complications in order to improve quality of life and to preempt further GI complications/

Relevance of the proposed work to the VA patient care mission

The VA system cares for a large number of persons with SCI, and FI and time consuming and cumbersome bowel care has been identified as a major QOL issue among the veterans. Despite extensive efforts to understand its pathophysiology and numerous clinical guidelines for its management, FI and constipation remain tenacious problems that limit the social interactions of veterans with SCI. The proposed work will result in the only known data regarding the efficacy of bowel biofeedback treatment and the outcome of FI in person with SCI. Furthermore, to the extent that biofeedback treatment can improve FI, this research should be cost effective because it would prevent physical and psychological comorbidities associated with neurogenic bowel as it is far less expensive to provide bio feedback treatment than to treat chronic conditions like depression arising from social isolation, and dermatological treatments arising from exposure of the skin to FI. Providing veterans with cutting edge preventive care is a key component of the VA patient care mission.

F. LIST OF KEY BIBLIOGRAPHICAL REFERENCES

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