Improvement of combat related Post Traumatic Stress Disorder (PTSD) symptoms, memory dysfunction and increased employability following Stellate Ganglion Blocks.

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Abstract

Objective: Report the successful use of stellate ganglion blocks (SGBs) in a patient experiencing symptoms of posttraumatic stress disorder (PTSD) as well as associated memory dysfunction.

Background: Efficacy of the SGB for the treatment of PTSD symptoms and memory dysfunction has been previously demonstrated. Considering the ever increasing number of patients with PTSD and memory dysfunction, we decided to evaluate the clinical effects of SGB in a patient with these symptoms.

Methods:

The patient was evaluated for diagnosis and symptoms of PTSD by the use of Post-traumatic Stress Disorder Checklist-Military (PCL-M). The memory function was evaluated by the use of and Rey Auditory Verbal Learning

Test (RAVLT). Both tests were administered on the intake visit to establish a baseline, and were repeated following each stellate ganglion injection. The patient underwent two right-sided SGB at the C6 level following the technique previously reported by our team. The SGB was administered by an anesthesiologist and the psychometric tests were administered by a neuropsychologist.

Results The patient experienced significant and durable relief of PTSD symptoms as measured by the PCL-M from a baseline score of 71, to a score of 40 following SGB #1. Following SBG #2, the patient's score dropped to 30, well below the cut-off score of 50 or above to diagnose PTSD. Similar improvement was noted with memory function, as measured by RAVLT, where the number of words recalled at least doubled.

Conclusion: Selective blockade of the right-sided stellate ganglion at the C6 level is a safe and minimally invasive procedure that may provide durable relief from PTSD symptoms and memory dysfunction.

INTRODUCTION

Post-traumatic stress disorder (PTSD) is a pathological anxiety condition with an increasing prevalence in military and civilian populations alike. Multiple factors may be responsible for this increase, among them are: large military operations, international terrorism, natural disasters, and increased awareness. Post-traumatic stress disorder is a chronic anxiety disorder caused by seeing or experiencing traumatic events. The symptoms of PTSD include re-experiencing the event through flashbacks or nightmares, avoidance of stimuli which remind the victim of the traumatic event, and increased arousal, such as anxiety, anger or hypervigilance. Beyond the above symptoms, memory dysfunction (MD) has been shown to be associated with PTSD in the past (1). This has been highlighted in the

follow-up study of veterans of World War II that showed many people still suffered from episodes of 'black-outs' or loss of explicit memory by Dr. Archibald in 1965 (2). Vietnam veterans with PTSD have shown deficits in short-term memory, as assessed with the Auditory Verbal Learning Test (AVLT), in comparison to veterans without PTSD (3). Veterans also manifested a significant decrease in the retention of previously presented material following exposure to an intervening word list (4). Symptoms of PTSD and memory dysfunction may lead to significant distress and functional impairment. Traditionally, medical treatments for PTSD have relied upon pharmacological agents and psychological interventions, such as exposure therapy and the like. However, the efficacy of these approaches have been limited (5). The memory dysfunction therapy has an even worse track record, where virtually nothing seems effective. However, a possible solution for the memory dysfunction and PTSD symptoms may be offered by the use of stellate ganglion block (SGB). Successful treatment of posttraumatic stress disorder (PTSD) symptoms with stellate ganglion block (SGB) has been reported previously (6,7, 8, 9). Equally, SGB has been successfully used to treat memory dysfunction due to organic brain syndrome in 1955 (10). Both of those directions of research motivated the authors to evaluate the effect of SGB on PTSD symptoms and memory dysfunction.

METHODS

Right-sided C6 Cervical Sympathetic Chain Blockade.

Once written consent was administered, a right-sided SGB was performed. An intravenous line was started with a 22G IV in the left hand. The patient was positioned comfortably in the supine position and prepped and draped in the sterile fashion. After radiographic confirmation of the right-sided C6

vertebral body, the skin was anesthetized with 2 cc of 1% lidocaine. Using an anterior paratracheal approach, a 22-gauge Quincke needle was passed under fluoroscopic guidance, until contact with the anterolateral vertebral body of the C6 was made, and the needle then pulled back 1 mm. Appropriate needle position was then confirmed by the injection of 2-4 cc of iohexol (180 mg/mL) radio-opaque dye to monitor its spread. After negative aspiration, a 0.5 cc test dose of 0.5% bupivacaine was injected. No side effects were noted after the test dose, so sympathetic blockade was then achieved by the slow injection of 6.5cc of 0.5% bupivacaine. We monitored the patient's right hand temperature for 15 minutes following the anesthetic administration to confirm successful blockade of the cervical sympathetic ganglia, as evidenced by an increase of at least 1.5°C. We also observed the patient for facial anhidrosis and Horner's syndrome (ie, enophthalmos, ptosis, swelling of the lower eyelid, miosis, and heterochromia) for further confirmation of sympathetic blockade. Both SGB's were performed by the primary author.

PSYCHOMETRIC TESTING

Two categories of psychometric testing were utilized: PTSD Checklist_-Military (PCL-M) to make the diagnosis of PTSD and its severity; Rey Auditory Verbal Learning Test (RAVLT) is a test that evaluates various memories and the rate of learning.

The PCL-M is a 17 item psychometric test commonly used to screen for PTSD. It was developed based on the PTSD criteria from the Diagnostic and Statistical Manual of Mental Disorders IV (11). The PCL's initial validation (12) found that it was an effective brief screen for identifying

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PTSD. The PCL has since been validated for screening troops returning from combat to identify those with PTSD (13), as well as assessing symptom improvement as a result of treatment (14). Optimal score for diagnosing combat related PTSD seems to be over 50 (14).

The RAVLT is a memory test where subjects are read a list of 15 words on 5 separate trials. RAVLT evaluates a wide diversity of functions including immediate auditory-verbal memory, recent auditory-verbal memory, and rate of learning. Reliability for RAVLT is significant as per Dr. Snow (15).

CASE REPORT

The patient was a 42 year old naval chief that worked on maintenance of air planes in Afghanistan as well as Iraq. He reported not being on the front lines. He does report having a traumatic event where he was involved in convoy in Iraq, however he did not want to provide details of that event. His symptoms included pronounced anxiety symptoms such as shortness of breath, heart palpitations, poor sleep, nightmares, poor memory function, as well as drinking 8 to 10 beers per day. He also considered himself "unemployable" due to his anxiety, memory dysfunction, and his high alcohol intake. His pharmacologic treatment at the time of first visit included citalopram 40mg ½ tab daily..

He returned for neuropsychologic testing (NPT), which were done to obtain baseline evaluation one week following the original visit. The patient then underwent SGB #1 one week following NPT, per the methods section with the addition of sedation. Thirty minutes after the block his skin temperature had risen 2°C indicating an appropriate sympathetic block, Horner syndrome was also noted. The patient's spontaneous comments following the block included the following: "I feel a lot better", "I have slowed

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down, but in good way". He then returned to the clinic 30 days following SGB#1 and reported marked improvement in PTSD symptoms. He also reported an improvement in memory function, which was confirmed by repeated NPT. Approximately 86 days after SGB #1 the patient spontaneously reported a partial relapse of his symptoms and requested a second SGB. This was done day 95 after SGB #1. The patient returned to the clinic 30 days following SGB#2, and once again, the patient reported an improvement in PTSD symptoms, as well as memory dysfunction. The patient stated he perceived the improvements as more pronounced following SGB#2 compared to the first procedure. This was confirmed by repeated PCL-M and NPT, and is demonstrated in Chart 1. At the time of this report (over 200 days after SGB#1) the patient remains essentially free from alcohol intake with markedly improved PTSD symptoms, improved memory, and most important from patient's perspective, he was able to find and hold a job in the construction industry. He spontaneously reported to the neuropsychologist that when the injections are effective, he stops drinking alcohol. "I just do not want it."

PCL-M Total Score

	Pre-Procedures	Post-Procedure#1	Post-Procedure#2
Total:	71	40	30

RAVLT

Pre-Procedures	**Post-Procedure #1**		**Post-Procedure #2**
Trial I:	3/15	6/15	6/15
Trial VI:	10/15	11/15	13/15
Delay:	5/15	7/15	12/15
Recognition:	9/15	12 /15	14/15

Chart #1

Interpretation of the results

PCL-M scores dropped 41 points in total across the three evaluations, with the cutoff range for diagnosis of PTDS being 50 (see above). Consequently, patient went from reporting symptoms sufficient to meeting the criteria for moderate to severe PTSD (i.e., 71) to a reduction of symptoms that no longer met diagnostic requirements (i.e., 40 and 30, respectively).

On the RAVLT each trial has a maximum score of 15, so if the patient recalled 3 of the 15 words it was recorded as 3/15.

Trial I measures immediate memory

Trial VI measures susceptibility to interference

Delay measures recent memory

Recognition measures recognition memory

DISCUSSION

Multiple mechanisms have been set forth to explain the onset of PTSD and memory dysfunction (MD) independently as well as reciprocally. Disruptive, vivid, emotional, and somato-sensory-intrusive memories are

hallmarks of PTSD (11). The key processes underlying this pathway are: 1) the primary consolidation of the initial trauma memory into long-term traces, and 2) its recurrent cue-triggered reactivation. Trauma, psychological and or physical, effect various mediators and neurotransmitters that have a significant effect on the multiple brain structures.

Brief overview of memory and related neuroanatomy.

Memory has multiple components and those components are controlled by different neurological structures: factual recall (declarative) is mediated by hippocampus, while emotional memory (non-declarative) is mediated by the amygdala. The amygdala is known to be active in PTSD and fear conditioning (16), as well as emotional memory (16). In a patient with bilateral loss of hippocampus and intact amygdale, the patients have been shown to be amnestic or lose declarative memory, however, the emotional memory appears intact (17). Stress hormone-induced activation of the amygdala regulates declarative memory storage in other brain regions (18). Thus, it seems that the amygdala is active in both types of memory.

Figure #1

Autonomic nervous system [ANS], sympathetic effect.

Neurobiological studies have shown that the noradrenergic stress-system is involved in enhanced encoding of emotional memories, sensitization, and fear conditioning, by way of its effects on the amygdale (1). Concentrations of ANS mediators (Norepinephrine) surge during acute stress and may persist following the acute stress (19). The amygdala is

activated by stress hormones, leading to increased emotional memory activation mediated by norepinephrine (NE) (18).

Chronic stress also affects the hippocampus, a brain area involved in declarative memories, suggesting that hippocampal dysfunction may partly account for the deficits in declarative memory in PTSD patients (1).

Chronic stress is associated with increased firing of noradrenaline neurons in the brainstem and potentiated release of noradrenaline in the brain with subsequent stressors (20). Since the experience of a stressful event might be accompanied by adrenaline release, the noradrenergic system may play an important role in the enhanced encoding of trauma related memories of PTSD patients. The loop can continue, thus enhancing the effect. Retrieval of a traumatic event is accompanied by adrenaline release, thus a positive feedback loop is set up. This view is confirmed by the finding of enhanced plasma NE in veterans with PTSD after exposure to auditory stimuli reminiscent of combat (21).

Figure #2

The amygdala has connections to the prefrontal cortex (PFC) (see figure #1). The PFC allows the inhibition of inappropriate cognitive and emotional responses or distracting stimuli (22). The PFC may also be involved in the modulation of the amygdala and emotionally charged memory, since exposure to stress increases catecholamine release in the PFC (23). Norepinephrine may have a dual effect on PFC, specifically: at high levels of NE, PFC function is impaired, while at low levels of NE, prefrontal cortex function is increased. This seems to occur due to NE having a higher affinity for alpha-2 receptors than for alpha-1 receptors, thus low levels of

NE activate alpha-2 receptors, activation of which reduces sympathetic system activity (24). At higher levels of NE, PFC dysfunction might account for working memory deficits of PTSD patients (19). There are several indications that the PFC also has a function in the inhibition of emotions through its projections to the amygdale (1).

As a first rapid reaction, NE is secreted. This may strengthen emotional memory traces, and enhance fear conditioning (1). (see figure #3)

Figure #3

The connection of the SGB and NE needs to be made to provide a possible explanation of the effect on PTSD and memory. The first step in that direction was made by Dr. Masataka who demonstrated that after SGB, the plasma concentrations of epinephrine and NE decreased significantly (25). Further detail in this direction is the fact that the stellate ganglion has been shown to have second order by pseudo-rabies virus neuronal tracing (26) to the amygdala (see figure #4). Another fact along the line of explanation is the role of nerve growth factor (NGF) in stress. NGF is known to increase with acute (*27*) and chronic stress (28) (*Smith MA 1996*). Increased concentrations of NGF causes sprouting (new nerve growth) at the end terminals (29) ,which in turn leads to increased NE output (30) as detected in elevated urine levels among those with PTSD (31) .

Finally, bringing the theory full circle is the evidence that a local anesthetic injected near a sympathetic ganglion leads to the reduction of NGF (32), which is essential for maintenance of new nerve sprouting (33). Thus SGB reduces NGF, which leads to a reduction of sprouting, leading to a reduction of NE, reversing or normalizing NE levels.

Figure #4

In summary, we believe the effect of SGB on declarative memory is due to the reduction of NE, which leads to activation of alpha-2 receptors, increasing memory function. This also reduces or stops the reactivation cycle fueled by NE. Further, it has been shown that PFC function increases, leading to inhibition of inappropriate cognitive and emotional responses.(22)

Conclusion. Fluoroscopic-guided SGB appears to provide significant relief of PTSD symptoms, as well as improve memory function and employability in the combat related disorder. We further believe further study of this approach is warranted considering the immensity of the PTSD and associated memory dysfunction problems surging in our society today.

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