

Evoked Potentials and Regional Cerebral Blood Flow Changes in Conversion Disorder: A Case Report and Review

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Abstract

Conversion disorder is defined as the presence of functional impairment in motor, sensory or neurovegetative systems which cannot be explained by a general medical condition. Although the diagnostic systems emphasize the absence of an organic basis for the dysfunction in conversion disorder, there has been a growing interest in the specific functional brain correlates of conversion symptoms in recent years, particularly by examining neuroimaging and neurophysiological measures. In this case report, regional cerebral blood flow changes and evoked potentials of a patient with conversion symptoms are presented. Somatosensory evoked potentials (SEP) of this patient with conversion disorder who had signs of movement disorder revealed that the latency to N20, P 25 waves were in normal limits while the amplitudes of the P25 and N33 components were extremely high (giant SEP). Regional cerebral blood flow assessment revealed hypoperfusion in the left parietal and temporal lobes of the brain. Three months after the first assessment, the control scans showed that the left parietal hypoperfusion disappeared while the left temporal hypoperfusion was still present. The following SEP evaluations which were repeated twice in three months intervals after the initial recordings, showed the persistence of the abnormalities in somatosensory measures. The neurophysiological and neuroimaging findings in conversion disorder were reviewed and the results of the evaluations of this case were discussed in this article.

Key Words: Conversion disorder, regional cerebral blood flow, SPECT, evoked potentials

INTRODUCTION

Conversion disorder (CD) is defined as the presence of functional impairment in motor, sensory or neurovegetative systems which cannot be explained by a general medical condition (Öztürk 2001). This disorder is classified in ICD 10 under “dissociative disorders” within the context of “dissociative impairment of motor and sensory systems”. (World Health Organization 1992).

It is included in DSM-IV as a diagnosis under the heading of somatoform disorders. (American Psychiatric Association, 1994). In both diagnostic criteria, the fact that the functional impairment observed should not stem from a medical disorder is emphasized. However, in recent years, there have been reports of pathological findings in brain function patients with findings of conversion disorder. These reports have led to focusing on

disorders that might have findings on brain imaging and neurophysiological testing that accompany conversion symptoms.

The first findings reported in brain imaging are functional changes seen in a patient that had conversive symptoms mimicking left hemiparesis (Marshall et al., 1997). In this patient, there was no increased activity in the right primary motor cortex that accompanied the effort to move the hemiparetic body half; however, there was increased activity documented in the right orbitofrontal and frontal cingulate regions. Yazici and Kostakoglu (1998) have performed brain SPECT imaging on 5 patients with movement disorders presenting as astasia-abasia and found that 4 patients had decreased regional blood flow in the left temporal region and one other patient had similarly decreased blood flow in the

left parietal region. Spence and colleagues (2000) have documented decreased activity in the left dorsolateral prefrontal cortex in patients with conversion disorders presenting as hemiparesis in functional brain imaging studies. In another study involving conversion patients with sensory-motor functional impairment, the thalamus, putamen, and caudate regions contralateral to the symptomatic body half had decreased regional blood flow. Investigators have reported improvement in blood flow accompanying improvement in symptoms (Vuilleumier et al., 2001). In another case report, infarct of the right parietal lobe has been reported to accompany the clinical picture in a patient with conversion disorder (Ramasubbu, 2002).

In patients with conversion disorders, studies on electrophysiological measurements have largely had negative findings. The few reports in the literature are conflicting and are not based on recent large scale studies with adequate sample size. Hernandez et al., (1963) have reported a case of absence of SEP waves in a conversion patient with loss of sensation in the arm. In another study, it is reported that when a patient with findings of hysterical hemiparesis was given a subliminal stimulus in the symptomatic body half, a decrease in amplitude of SEP waves occurred while SEP waves remained symmetrical with supraliminal stimulus (Levy and Mushin 1973). Flor-Henry et al. (1981) have performed neurophysiological testing on patients with symptoms of conversion disorder and have reported impairment in both the dominant and non-dominant hemispheres that were more pronounced in the dominant side. In addition to these, Yazici et al. (2004) have reported inability to detect normal somatosensorial potentials in disease activation, with restoration of normal SEP responses after the resolution of symptoms in two conversion patients (Yazıcı et al., 2004). In another study conducted in our country, event related auditory evoked potentials were studied in a group of patients with conversion disorder manifested by various neurological symptoms. According to these results, N1 and P2 latency times were prolonged compared to the control group with decreased amplitude of P 3 (Köse et al., 1998).

Despite the presence of these scarce positive findings in the literature, negative conclusions predominate (Kaplan et al., 1985; Foong et al., 1997; Haghighi et al., 2001; Ramassubu, 2002). The studies that belong to this latter group support the notion of absence of pathological evoked potential findings as a diagnostic parameter in conversion disorder.

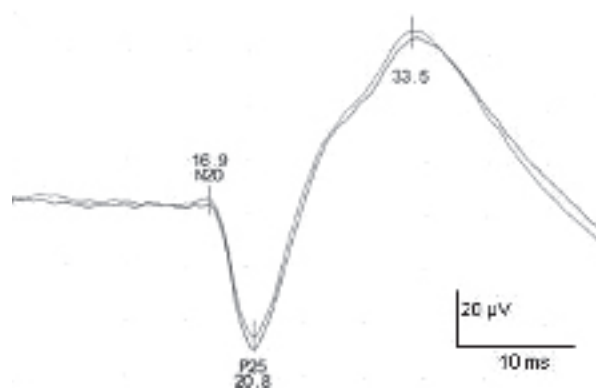
In this report, the changes in regional blood flow and evoked potentials found in a patient with conversion symptoms is presented. Informed consent was obtained prior to pursuing work-up.

Case: A 21 year old female, single, unemployed patient. She lives in Artvin with her family. The initial symptoms reported are tremor and loss of balance while ascending stairs that started five years ago. These symptoms have recurred several times at one-to-two month intervals. Thereafter, they were more persistent. Initially, no difficulties in ambulation were reported however, over time walking became difficult. She reports frequent falls or the need to support herself by grabbing onto furniture while walking. When faced with another person approaching her from the opposite direction, her imbalance increased and she experienced tremors of the whole body. She had difficulties turning over in bed while sleeping. She could not get up from her bed without support in the morning. When she had to go up the stairs, she had leg trembling and could not keep her balance. Therefore, she was home-bound for most of the time and also had difficulties with daily household chores. Her complaints increased when she was tired. Sometimes hand tremors were also superimposed on difficulties in walking and balance.

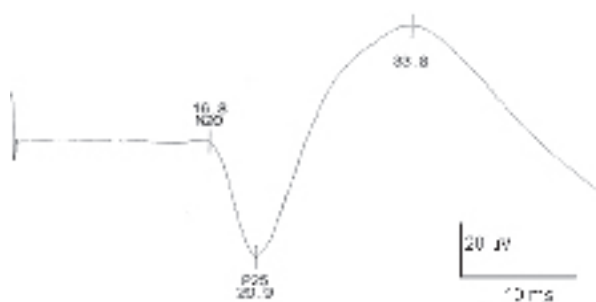
The patient was evaluated by neurologists in the area she lived in. Brain magnetic resonance imaging was reported to be within normal limits. Since no improvements in her complaints were seen over time, she presented to Hacettepe University Medical School Neurology Outpatient Clinic.

On initial evaluation in the outpatient clinic of our center, she was found to have no other significant neurological abnormalities other than difficulty in walking. The reported symptoms were not compatible with any known neurological disorder therefore, she was referred to the psychiatry clinic with a working diagnosis of conversion disorder. Her initial evaluation in the psychiatry clinic concurred with the same assessment and she was hospitalized in the psychiatry clinic for further treatment.

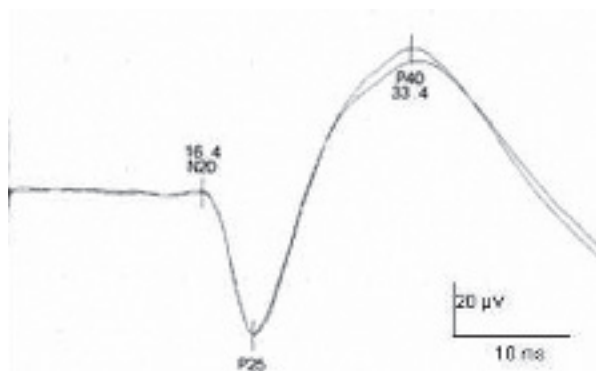
On admission to the psychiatry ward, the patient had significant difficulty in walking. She experienced frequent falls and had to grab for support. Despite the fact that ambulation problems interfered with her daily life, she was noted to be in a state of partial emotional detachment about the difficulties she was going through. Physical examination findings were within normal limits. On neurological examination, cranial nerves were



A.



B.



C.

Figure 1 A-B-C: Pre- and post-treatment SEP findings: In the first SEP evaluation (1-A), N20 and P25 wave latencies were within normal limits, however, peak amplitude of P25-N33 was observed to be very high (giant SEP). It was observed that amplitude gradually ascended higher in the assessment made in the 3rd (1-B) and 6th months (1-C) following discharge from hospital.

intact, motor and sensory examinations were within normal limits. All reflexes were normal. There were no pathological reflexes.

On psychiatric examination, she was alert and cooperative. Her general appearance was compatible with

her age and socioeconomic status. Her speech was at a normal rate and tone. Even though she was unhappy, there were no signs of depression. There were no perception problems. Thought process was normal. She did have concerns about her disease. Physical examination was within normal limits. A complete blood count, routine chemistries, thyroid function tests, serum vitamin B 12 levels, folic acid levels, urinalysis did not reveal any abnormalities. EEG was within normal limits. With normal findings on brain imaging studies (MR) conversion disorder was diagnosed. The first evoked potential (SEP, MEP) measurements and regional blood flow assessments (SPECT) were performed concurrently.

While an inpatient in the psychiatry ward, the patient underwent supportive psychotherapy that focused on conflict areas and also was started on sertraline (50mg/day). She also received physical therapy in order to help her acquire physical abilities to cope with ambulation problems. During her stay in the hospital, she was noted to have more episodes of loss of balance and falls around health care personnel. Further interview revealed that she was sexually abused by a relative two years older than herself when she was seven years old. Patient reported feelings of guilt and concerns about the future related to this incident. Furthermore, it was learned that when patient was 8 years old her father suffered an accidental gunshot wound and the patient felt sorrow about this event.

While the frequency of the balance problems and falls waxed and waned throughout the day, in general the frequency decreased. During her initial stay, her legs trembled when walking and she had to grab for support and sometimes collapsed. These episodes recurred 3-4 times a day. However, after several weeks, she was noted to have less tremors and better balance. The number of falls decreased to a couple of events per week. In addition, though she could not keep her balance upon turning while walking initially, later on she was able to handle turns better. In her initial days in the ward, she had a wide based gait and walked with support, over time, she was noted to have a quicker pace with normalized gait. She initially could not climb stairs or could only do so with assistance, during her stay she could climb stairs slowly on her own and could perform the physical therapy exercises better. After eight weeks of hospitalization and improvement in imbalance and fall complaints, the patient was discharged to continue outpatient follow-up.

At discharge, the patient was given a daily exercise

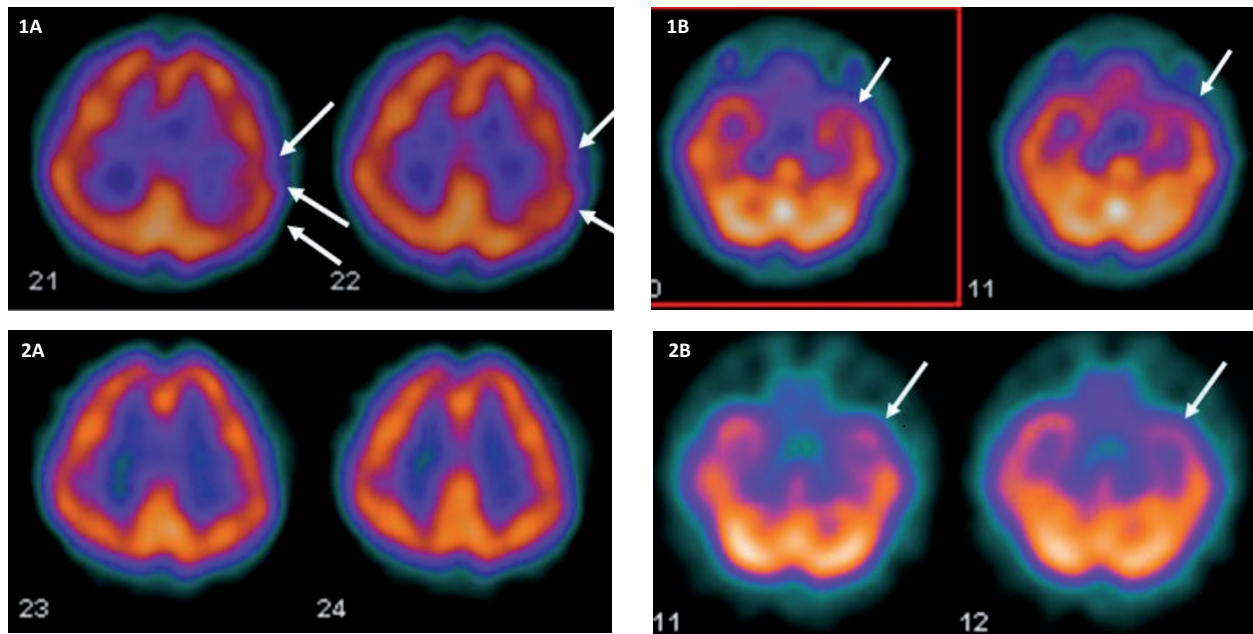


Image 1 A-B, 2 A-B: Images of pre- and post-treatment regional blood flow of brain: A decrease in perfusion is observed in the left parietal (1-A) and left temporal (1-B) regions in the pre-treatment period. It was found that treatment resulted in recovery of decrease of perfusion in the parietal region (2-A) though decrease of perfusion in the temporal region continued (2-B).

regimen by the physical therapist. The patient and her family were educated about the disease and behavioral recommendations were given. On a follow-up visit 10 days after hospital discharge, she reported no episodes of falling, she could help her mother with housework, could get in cars without support. She performed her daily exercise regimen regularly. The family could only come for follow-up every two months for transportation problems. In a follow-up visit two months after, she reported increased episodes of falling; however, she had days when she was free of any symptoms. On her good days, she could help her mother with housework and could walk out to the fields with her mother's assistance. In further visits, she had increased complaints such as reluctance and joylessness and appeared depressed during the interview. She expressed pessimism for failure of complete resolution of her walking problems. The sertraline dose that was started during her hospitalization was increased to 100 mg/day. During follow-up, the family lost their home to a fire with an undetermined cause and she had to stay with her relatives and her depressive symptoms increased. Thereafter, the patient's falls started increasing. She became homebound and was not able to perform any chores around the house. Sertraline was stopped and venlafaxine was started at 150 mg/day. In a follow-up visit one month later, lithium was added for failure of improvement in symptoms. The most recent visit was two months ago. Complaints of reluctance, joy-

lessness, and frequent crying had decreased. However, she still experienced ambulation problems. She reported being unable to do housework, dropping plates when she attempted to wash the dishes, and tripping on the carpet and falling. Her hands trembled when she ate and she spilled food on her clothes. She could go to the bathroom only with her mother's assistance and could not leave the house alone. She was advised to stick to the daily exercise regimen and to continue to attempt doing house chores. The patient is still being followed at two-month intervals.

(Since publication of this article in The Turkish Journal of Psychiatry (March 2007), the patient was seen for another follow-up appointment. She reported marked improvement in ambulation problems. Depressive symptoms had almost completely resolved).

Electrophysiological Studies and Findings

Somatosensory evoked potentials (SEP): With complaints of difficulty in ambulation and imbalance, in order to rule out a posterior cord involvement, somatosensory evoked potentials were obtained (SEP). For this, the right median nerve was stimulated continuously with surface electrode stimulators with stimulations of 0.2 msec at a frequency of 2 Hertz at the level of the wrist. SEPs were recorded from the opposite parietal sensory cortex (C3). The average of two hundred stimulations

was taken and this process was repeated two times. The average of the two results was reported.

The first SEP assessment was performed during hospitalization. In this test, while the latency of N20, P25 waves and the amplitude of N20 were within normal limits, the peak amplitude of P25-N33 was very high (giant SEP). Two more SEP studies were performed in the following 6 month period when her symptoms had partially abated. In these tests, the amplitude of P25-N33 was found to increase as 87 μ V, 103.9 μ V, and 113.5 μ V, respectively (Figure 1. A-B-C).

Based on these results, the following electrophysiological procedures—used to study motor control and movement disorders—were performed.

Event related potentials: Standard oddball paradigms were used. Frequent tones were given at regular intervals, rare tones were randomly given, recording were made from Cz and Pz electrodes. The recording was repeated twice. In both recordings, the latency of the P300 wave was within normal limits (330 ms).

Movement related potentials: The patient was shown how to do sudden abduction movements in the second right-hand finger intentionally and irregularly (almost every two seconds). While the patient was performing the described exercise, EMG was recorded from the right first dorsal interosseous muscle using concentric needle electrodes, and EEG was recorded in the Cz and C3 electrode positions. Rectified Emg signal was used as a trigger potential. EEG signals triggered after the start of the EMG signal, in an analysis window starting 2 seconds before and 500 ms after, were averaged using the “back-averaging” method.

The amplitude and latency periods of the movement related potentials obtained were within normal limits.

Transcranial Magnetic Stimulation (TMS): Medtronic MagPro magnetic stimulation device was used for transcranial magnetic stimulation, recordings were obtained from the first dorsal interosseous muscle with surface electrodes. With TMU, supraliminal stimulus was exercised during voluntary contraction and the interruption in the in the voluntary EMG activity (the silence) was calculated. The silent period was within normal limits (264 ms). In addition, conditioning stimulus was exercised at 75% of motor threshold level without causing MEP response, the test stimulus was exercised at 120% of the motor threshold with 1,2,3,4,5,6,7,9,12,15 ms interstimulus intervals and using double stimulation, intracortical inhibition and facilitation was investigated.

With double stimulation and interstimulus interval 1-5 ms, there was decrease in response amplitude compared to the control (inhibition) and increased amplitude over 7 ms (facilitation). These findings were deemed to be within normal limits.

Regional Brain Blood Flow (SPECT) Finding

In the evaluation of regional blood flow, perfusion SPECT (Single Photon Emission Computed Tomography) was performed. The patient underwent SPECT study twice, once before treatment and once three months after treatment.

For brain SPECT study, the patient was kept in a dark and quiet room for five minutes, then the brain perfusion agent named Tc-99m ECD (“ethyl cysteinate dimer”, “Neurolite, Bristol-Myers Squibb”, Belgium) was injected intravenously at a dose of 555 MBq. Fifteen minutes after injection, brain perfusion SPECT imaging was performed with a double headed SPECT gamma camera (Siemens, E-CAM, Erlangen, Germany) (high resolution, parallel hole colimator, 360 degree rotation, 128 x 128 matrix, 128 x 40 seconds imaging)

Pretreatment SPECT demonstrated moderately reduced regional brain blood flow (hypoperfusion) in the left parietal and left temporal lobes (Figure 1A-1B). The blood flow patterns in the other cortical and subcortical regions and in the cerebellum were normal. In the second SPECT imaging performed three months after the treatment, the decreased blood flow in the left parietal region seen in the first scintigraphy was normalized, the hypoperfusion in the left temporal region persisted (Figure 2A-2B).

DISCUSSION

The SEP findings of increased P25-N33 amplitudes observed in the symptomatic phase also persisted at follow-up visits. In the literature, giant SEPs seen in different patient groups have been associated with increased sensitivity of the primary sensory cortex and intracortical disinhibition (Kofler et al., 2000). Giant SEP findings were most frequently found in patients with cortical reflex myoclonus and the physiopathology was investigated in these patients. In this study, giant SEPs were thought not to be an abnormal compound of potentials but to originate from excessive increase in the psychological components of normal SEPs (Shibasaki and Hallet 2005). Increased sensitivity was thought to occur from the primary somatosensorial cortex and the regions of 3b—which takes input from touch sensation-

and 3a -receiving proprioceptive input. In this patient group, similar to our patient, there was an increase in the amplitude of the SEP components with shorter latency originating from the subcortical regions. On the other hand, in TMU studies, there was no increased intracortical sensitivity of the motor cortical regions or decreased inhibition for the parameters tested.

Similar SEP findings have not been reported in patients with conversion disorder before. In the differential diagnosis of the presenting symptoms of movement disorders like tremors and jerking that increased with activities like walking or climbing stairs, there were no findings that supported cortical myoclonus in our patient. On the other hand, it is interesting to note that as mentioned above, the sensory-motor cortical sensitivity changes and giant SEPs that are found in cortical myoclonus were also found in our patient who presented with similar symptoms.

The brain imaging performed in the symptomatic period in our patient has demonstrated a moderate degree of hypoperfusion in the left parietal and temporal regions. With partial ablation of symptoms, there was an improvement in the blood flow of the parietal region, the temporal hypoperfusion persisted. In addition, the increased amplitude of P25-N33 waves found in the initial SEP evaluation persisted during follow-up.

Yazici and Kostakoglu (1998) have reported similar findings of relatively decreased blood flow in the left parietal and temporal regions in the active phase of the disease. However, since there was no follow-up SPECT imaging performed in this study, there is no correlation that can be discussed between the course of the symptoms and the blood flow changes. Vuilleumier et al. (2001), have reported decreased blood flow in the contralateral thalamus, putamen and caudate nuclei in a group of patients with conversion disorder. In this study, improvement in brain blood flow that accompanies improvement in clinical findings is reported. In the case presented here, the regional blood flow in the thalamus and basal ganglia were symmetrical and normal.

The findings from brain functional imaging studies reported in the literature do not adequately explain the physiopathology of conversion disorder. Marshall et al. (1997) have construed the lack of increased activity in the primary motor cortex and the presence of increased activity seen in the right orbitofrontal and frontal cingulate regions which accompany the attempt to move the hemiparetic body half to the possibility that these brain structures may have an inhibitory effect on the

motor cortex. Interestingly, Halligan et al. (2000), have shown increased activity in the contralateral orbitofrontal and frontal cingulate cortex in a patient experiencing paralysis under hypnosis that accompanied the effort to move and extremity. Investigators have deduced that the physiopathological processes in conversion disorder and hypnotic-paralysis are similar.

Vuilleumier et al. (2001) have shown that the regional blood flow changes in patients with conversion disorder symptoms are not restricted to the cortical structures. The investigators have observed decreased blood flow in the thalamus and basal ganglia contralateral to the symptomatic side in their cohort of patients with impaired sensorial and motor function and have proposed a role for the circuit of the striatum-thalamus-cortex (striatothalamocortical circuit) in conversion disorder. Emotional stressors are proposed to cause motor movement disorders by inhibiting this circuit via stimuli originating from amygdala and orbitofrontal cortex. It is interesting to note that there was a relation demonstrated between blood flow of the caudate nuclei and termination of symptoms.

Spence et al. (2000) have observed decreased activity of the left dorsolateral prefrontal cortex during motion in patients with conversion disorder. In this same study patients who mimicked paralysis were also investigated and in contrast to the patients with conversion disorder, there was no decreased activity of the right prefrontal cortex. The investigators have suggested that the dorsolateral frontal cortex is one of the primary centers for higher voluntary movements and there is a difficulty in performing these voluntary movements in conversion patients.

Another aspect that needs to be taken into consideration in the evaluation of the regional brain flow findings is that the regional blood flow changes that accompany psychiatric disorders do not always reflect specific disease-related pathophysiological processes. Some of the regional blood flow changes could be a reflection of other processes that surface secondary to primary disease (such as anxiety) or manifestations of the mechanisms that come into play in the organism in the adaptation to psychological-physical stress. Therefore, the clear explanation of the findings encountered in our patient would only be possible with controlled larger-scale studies.

The cumulative findings in the case presented here lend support to the other study findings that suggest significant brain changes in patients with conversion disorder. The potential future impact of such findings

would be on the definition of conversion disorder in the diagnostic systems. The absence of organic findings that could explain the clinical picture is still considered a diagnostic parameter in conversion disorder. Without doubt as reports like ours accumulate, the distinction between medical -functional disorders will become blurred.

Finally, in the case presented here, there were some characteristics in symptom choice that could be significant. The patient's father suffered accidental injuries to

his left arm and leg and as a result walked dragging his left foot and had problems with balance. The patient was a close witness to the hardships her father was going through and was deeply impacted by this. Other studies and clinical observations have shown that 'symptom choice' in conversion patients is frequently modeled after physical complaints seen among their close relations. This observation might have been valid in our patient as well.

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