

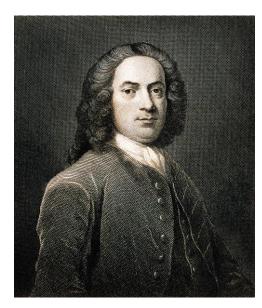
Prof. Manoel Jacobsen Teixeira Department of Neurology University of São Paulo Medical School



- •Brachial plexus Injury Galen 1st aD
- •Birth-related brachial plexus palsy (obstetric brachial plexus paralysis) Smillie1764
- Non-birth-related brachial plexus palsy *Flaubert 1827*
- •Dorsal and ventral brachial plexus root avulsion Adson 1922
- Lumbosacral plexus avulsion Nosik 1955



Claudius Galenus 129-199



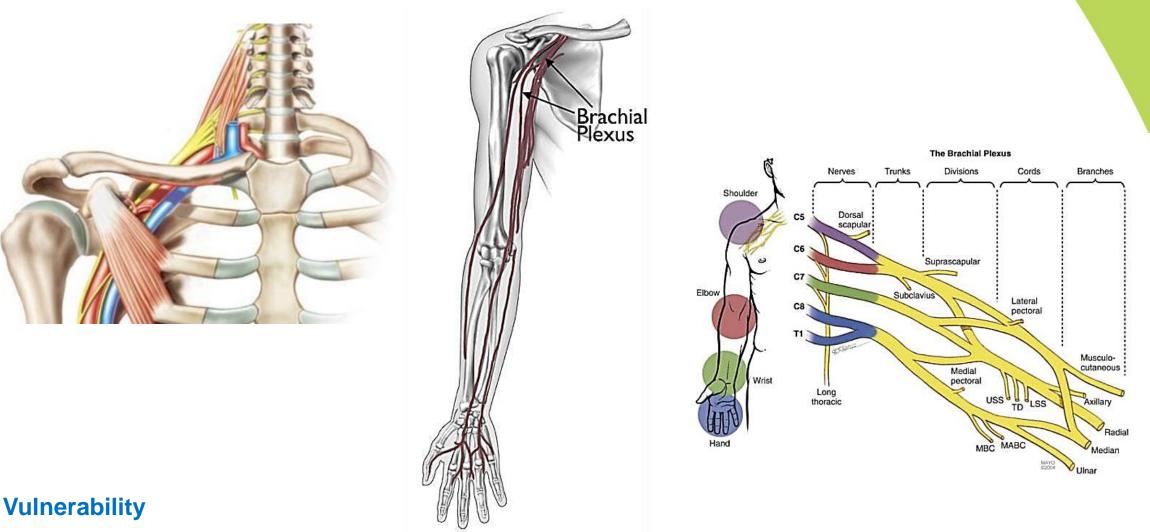
William Smillie 1697 - 1763



ce of Smellie's Traité de la Theorie et ratique des Accouchemens (Treatise on the Theory and Practice of Delivery), French translation, Paris, Theofile Barrois, Libraire, 1771



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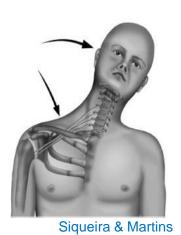


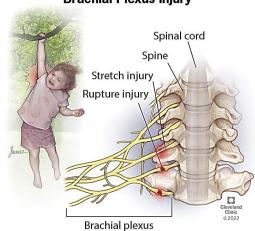
- Dorsal root lacks epineurium and endoneurium
- Low complacence of cervical roots: shorter length and angulation predisposing to mechanical stretching
- Greatest structural fragility in the dorsal root entry region in the spinal cord *Benjamin 2005*

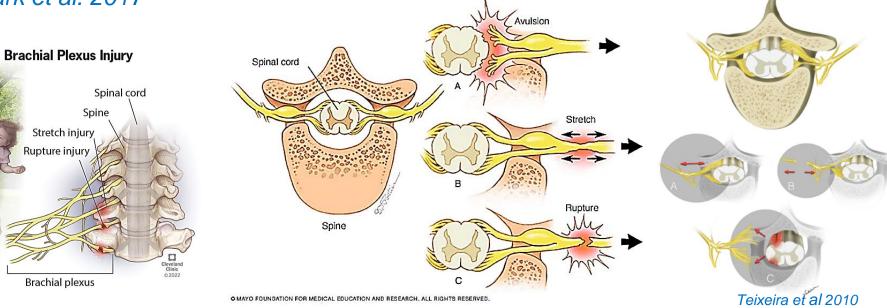


Classification of Brachial Plexus Lesion

- Preganglionic lesions (root avulsion): discontinuation at their junction with the spinal cord
- Postganglionic lesions: rupture or discontinuity of nerve tissue distal to the dorsal root ganglion`and or of brachial roots, plexullar trunks, divisions or nerve branches entrapment by scar tissue
- Combination of lesions Park et al. 2017 ٠







High-energy trauma to the upper extremity and or neck

Roots:	Axonopraxia
	Axonotmesis

Brachial plexus:

Neuropraxia Axonotmesis **Neurotmesis**



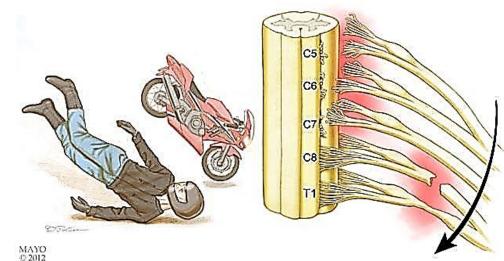
• Brachial plexus birth injury: 0.4–5.0/1,000 births *Lindqvist et al. 2012*

•Traumatic brachial plexus injuries: 1% of patients involved in major trauma *Midha 1997*

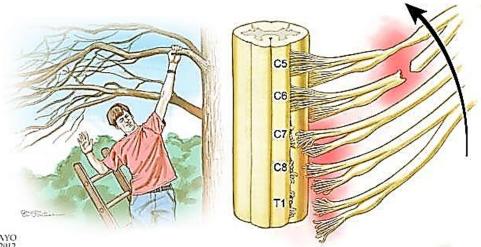
•Upward trend of occurrence *Dubuisson & Klin, 2002*







Violent distraction of brachial plexus nerve structures

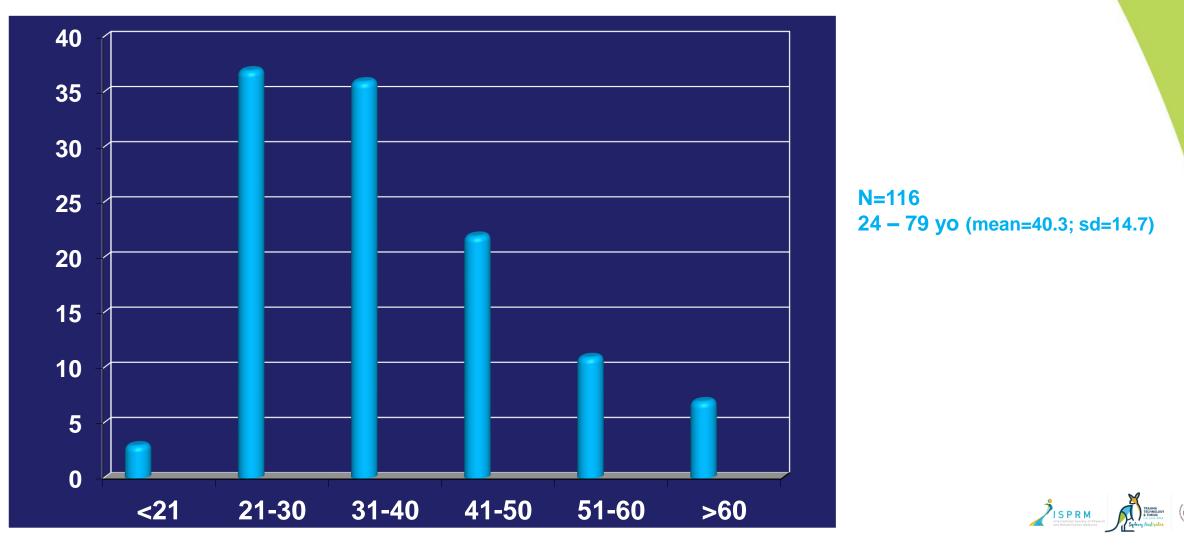


Trauma	%
 Motorcycle accident 	66.1
•Car accident	14.3
•Trampling	14.3
 Industrial/spotrs/domestic 	5.0

ISPRM International Society of Physical and Ruhabilitation Medicine

•70% moto-vehicles accidents•70% motorcycles or bicycles *Narakas 1985*

- Mean age of 26.4 yo
- Male 90.5%
- High social cost: man-hours of work lost by the patients and man-hours of caregivers work.
- Total indirect cost \$1,113,962 / patient over the postinjury lifetime *Hong et al. 2019*



Patients age range

BPA in BPI patients

Author(s) /year	Country/City	BPA in BPI series
Stevens 1934	USA - Boston	4 (3%) / 135
Tracy e Brannon 1958	USA -San Antonio	9 (69%) / 13
Davis 1947	USA -Chicago	2 (11%) /17
Bonney 1959	England - London	13 (45%) / 29
Taylor 1962	USA - Los Angeles	3 (50%) / 6
Yeoman & Seddon 1963	England - London	86 (48%) /180
Zorub 1974		21 (30%) /70
Ishijima 1988	Japan	19 (54%) / 35
Thomas & Sheehy 1988	England - London	19 (100%)
Birch 1996	England - London	148 (<mark>12%)</mark> / 1162
Htut 2006	England – London	76 (100%)
Flores 2006	Brazil - Brasilia	16 (<mark>76%)</mark> / 20
Ciaramitaro 2010	Brazil - Sao Paulo	2 (10%) / 7
Bertelli 2011	Brazil – Florianopolis	64 (42%) / 150
Jain 2012	Índia – Tamil Nad	70 (23%) / 304
De Moraes 2015	Brazil - Goiania	10 (21%) of 48
Zhou 2016	China - Shanghai	30 (100%)
Bertelli 2017	Brazil - Florianopolis	257 (45%) / 512
Patroclo 2018	Brazil - Rio de Janeiro	50 (44%) / 114
Clifton 2018	USA – Mayo Clinic	74 (16%) / 454

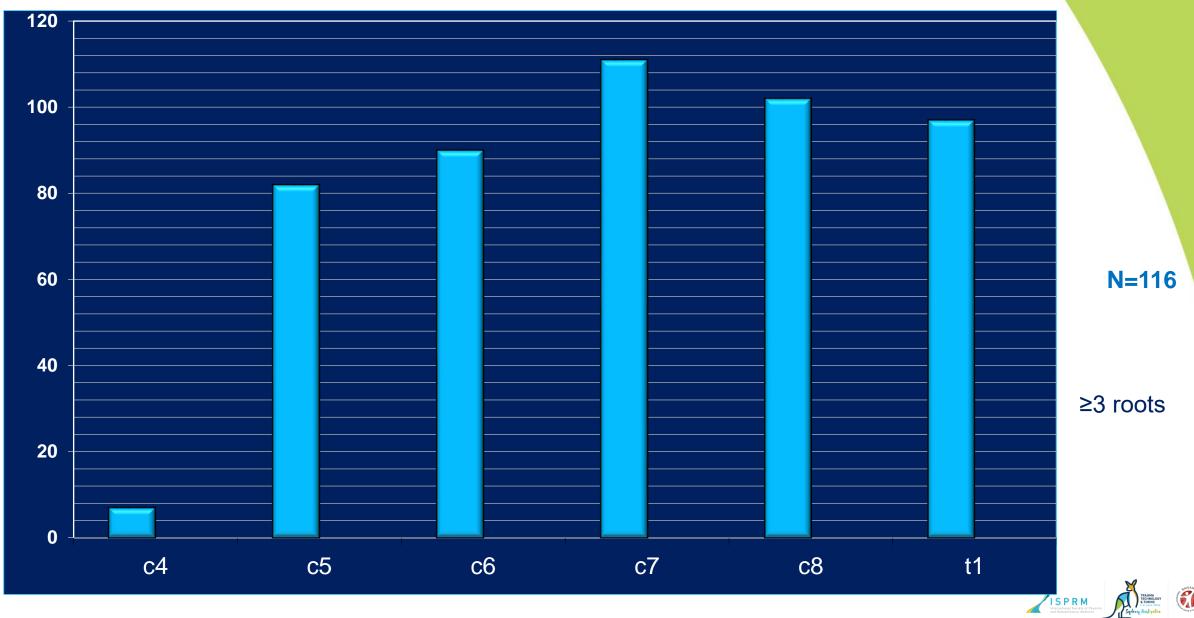
•Upper limb amputation: *50–85%*

- ► chronic pain: 54–87%
- ▶ phantom limb pain

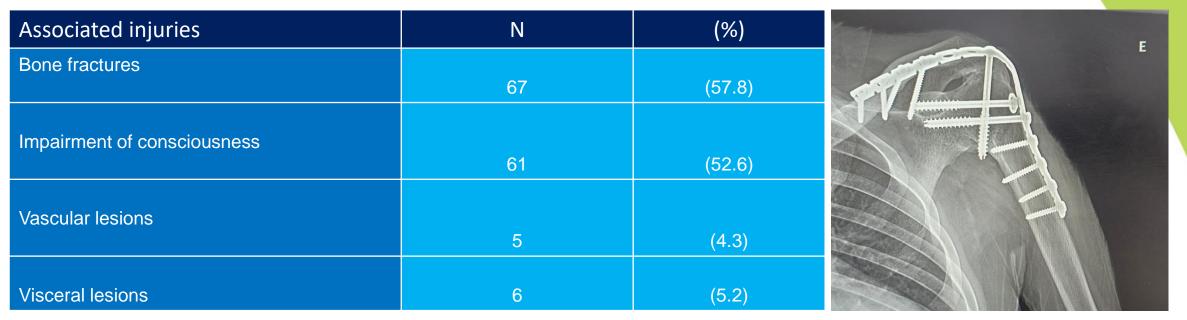
•CRPS: 21%



Cervical roots avulsed



Other traumatic lesions

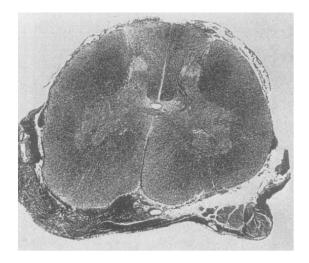


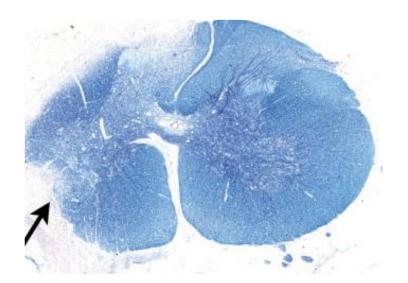
N=116

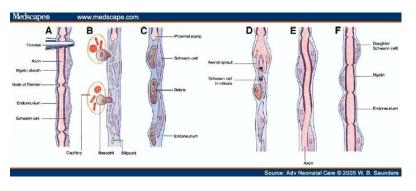
Associated orthopedic lesions	Ν	%	Surgery just after admission to the ER 49%	Ν	%
Hand	4	(3,4)			
Forearm or upper arm	26	(22,0)	Thoracic and/or abdominal	6	(5,2)
Lower limb	19	(16,4)		_	
Shoulder or shoulder girdle	1	(0,9)	Neurosurgery	7	(6,0)
Pelvis	4	(3,4)		00	
Ribs	6	(5,2)	Orthopedic	29	(25,0)
Jaw	4	(3,4)	Vascular	5	(4,3)
Vertebrae	4	(3,4)	Vasculai		(4,3)
Traumatic lower limb amputation	2	(1,7)	Total	47	(100,00)
Total	70	(100,0)			are nonsitivities reaction - July Spleen the System

•Motor, sensory, and sympathetic disturbances upper limb, shoulder, and or diaphragm motor déficits, arreflexia..: 100%

- •Autonomic disturbances: Claude Bernard-Horner's (64.0%)*, temperature, upper limb vascular perfusion.....
- •Sensory negative symptoms and or signs: nociceptive, tactile and or termal anaesthesia or hypoesthesia
- •Positive sensory symptoms and or signs: neuropathic, nociceptive, nociplastic and mixed pains, hyperalgesia & allodynea, Tinel-Hoffman's
- sign over the cervical or proximal upper limb (74.6%)*
- •Dysthrophic sequelae: skin, subcutaneous tissue, muscleskeletal structures and vesels Simon et al. 2015









- •Dysfunctions deficits. and disabilities
- •Impairment of self steen

- Use of slings 58.9%
- Scoliosis 80.4%

QoL impairment

	%
•Pain	64.3
 Motor deficit 	14.3
 Pain and motor deficit 	8,9
•Other	8,9

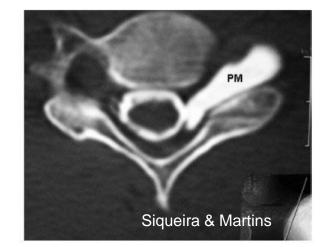




















Grade of upper limb functionality

DASH	Right upper limb	Left upper limb
Minimum	84.1	18.3
Maximum	1.6	76.6
Mean	43.0	47.3
SD	26.8	29.1

N=116

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•Prevalence: 70% of the patients Bonnard & Barakas 1985, Brussels 1988, Zhou et al. 2016

•Severe 10%-25% of the patients

•The most important complaint: 10%-90% of the patients Zorub et al. 1974

•Higher occurrence: number of (superior avulsed) roots, older patients Htut 2006,

•Less common in C8-T1 avulsion Bertelli et al. 2011

•Predisposing factors: alcohol abuse, smoking, psychiatric co-morbidities, marital status Saiz-Sapena et al.

•Time life occurrence and intensity: spontaneous progressive improvement ► 30% 3 years later

•Temporal presentation: acute / chronicle

•Quality of neuropathic pains

- Constant: tingling, burning, crushing, tearing, throbbing, pulling...

- Paroxysmal: shooting, electric shocks/ seconds - minutes Naraka 1979, Teixeira et al. 1999



Pain aetiologies & mechanisms

Aetiology of pain

- Neuropathic *Simon et al. 2015*
 - Peripheral nervous system: brachial plexus trauma Davis et al. 1947
 - Central nervous system: root avulsion Teixeira 2005
- Non-neuropathic pains
 - Musculoskeletal: osteoarticular, myofascial
 - Other organs
 - Unrelated
 - Psychogenic"/nociplastic



Mixed pains



• Neuropathic pain: 67%

Severe dysfunctions and disabilities and impairment of social integrity

• Non-neuropathic pain: 33% *Ciaramitaro et al. 2010*



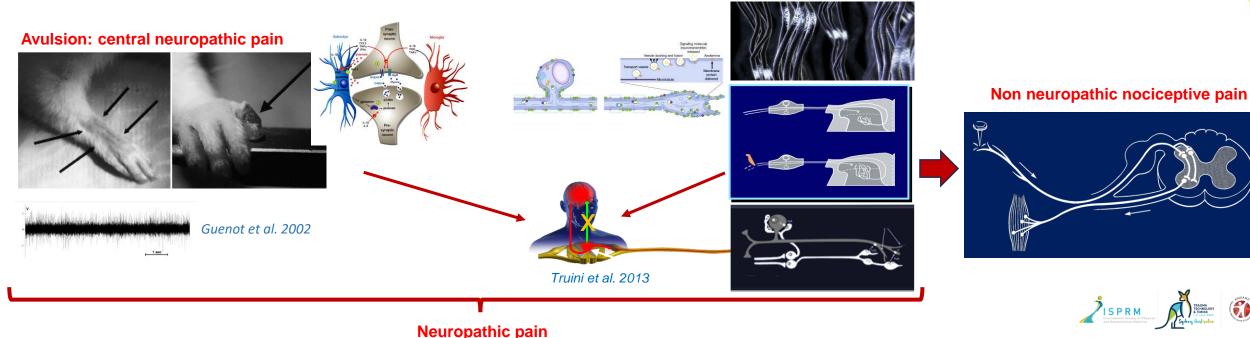
•Neuropathic pain (NeP): "pain arising as a direct consequence of a lesion, or disease affecting the somatosensory system" Treede et al., 2008

• Avulsion > central neuropathic pain: lesion between the root entry point into the spinal cord to 2 mm deep into the DH

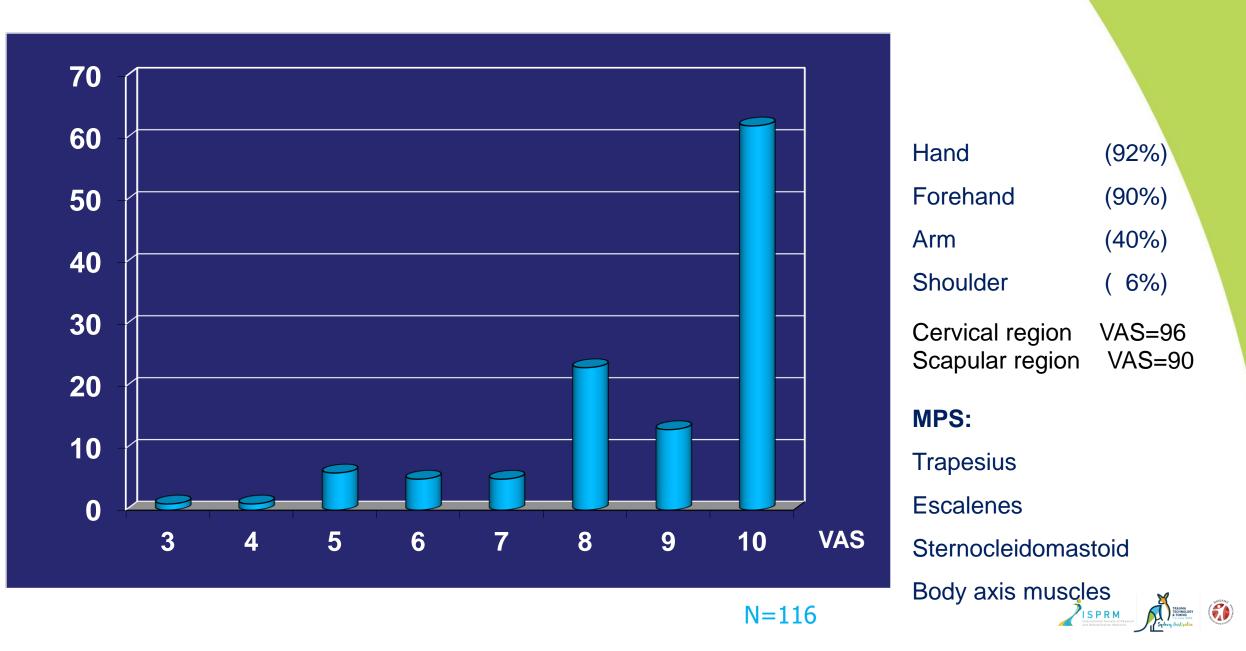
(laminas I - IIe) Teixeira, 2015, Mohanty et al. 2016, Sindou 1974, Guenot et al. 2003

- •Traumatic plexopathy > peripheral meuropathic pain: post-ganglonar ectompic potentials, ephatic currents, sympathetic abnormalities
- •Desinhibition of nociceptive DH neurons *Naraka 1979, Parry 1980, Nashold 1988, Teixeira et al. 1999* •Sprouting of intact fibers
- •Glia activation: release of chemokines and pro-inflammatory cytokines > pain signaling (CGRP, sP, glutamate) Paszcuk et al. 2011, Zhong 2021
- •Microglia ► proinflammatory cytokines: maladaptive neuroplasticity BDNF activity *Huang et al. 2021*
- •Sensitisation and neuroplasticity of supraspinal neurons

Traumatic plexopathy: peripheral neuropathic pain



VAS Pain scores



Predominant location of pain

The most frequent localizations of neuropathic pain: hand, wrist, forearm, and elbow *Bonney* 1959

Location of pain		_eft	Right		Total		NL 11C	
	N	(%)	N	(%)	N	(%)	N=116	
Hand, forearm	18	(15.5)	34	(29.3)	52	(44.8)		
Hand, forearm, arm	22	(19.0)	16	(13.8)	38	(32.8)		
Hand	1	(0.9)	7	(6.0)	8	(6.9)		
Hand, forearm, arm, cervical	2	(1.7)	1	(0.9)	3	(2.6)		
Hand, forearm, arm, shoulder	1	(0.9)	1	(0.9)	2	(1.7)		
Hand, forearm, arm, shoulder, chest	1	(0.9)	-	(0.0)	1	(0.9)	Neuro	
Hand, forearm, upper arm, chest	-	(0.0)	1	(0.9)	1	(0.9)	Mixed	
Hand, forearm, shoulder	-	(0.0)	1	(0.9_	1	(0.9)	Neck	
Shoulder, arm	-	(0.0)	1	(0.9)	1	(0.9)	Dorsal	
Shoulder, arm, forearm, hand	1	(0.9)	-	(0.0)	1	(0.9)	Whole	
Shoulder, hand, forearm	-	(0.0)	1	(0.9)	1	(0.9)	Low ba	
Arm, hand	1	(0.9)	-	(0.0)	1	(0.9)	Pector	
Arm	-	(0.0)	1	(0.9)	1	(0.9)	Head	
Forearm, arm, hand, cervical	1	(0.9)	-	(0.0)	1	(0.9)		
Forearm, arm	1	(0.0)	1	(0.9)	1	(0.9)		
Foot	1	(0.9)	-	(0.0)	1	(0.9)		
Foot, knee	-	(0.0)	1	(0.9)	1	(0.9)		
Foot, leg	1	(0.9)	-	(0.0)	1	(0.9)		
Total	50	(43.1)	66	(56.9)	116	(100.0)		

	(%)
Neuropathic pains:	44,1
Mixed pains:	55,8
Neck	28.6
Dorsal region	19.6
Whole Back	14.3
Low back	12.5
Pectoral region	8.9
Head	7.1



PI	hantom sensations	83.3%
•	Static	81,0%
•	Dynamic	54,8%.
•	Perception of movement during sleep	75.0%
•	Phantom limb touchingipsilateral hemiface	16.3%
•	Dysmorphometry Limb shortening	16.1%
	Limb stretchig	37.5%

Interval between the appearance of phantom limb pain and the injury ifis is a set in the injury first week 3 (15.8) 7 first 6 months 3 (15.8) 7 more then 6 months 3 (15.8) 7 Still has phantom limb pain 13 (68.4) 5 No 3 (15.8) 7 Yes 16 (84.2) 1 Phantom limb pain frequency 5 6 Sometimes a year 2 (10.5) 6 Daily 8 (42.1) 6 No applicable 3 (15.8) 5 Phantom limb thermal sensation (burning / freezing) 7 36.8 No 12 (63.2) 1 Yes 6 (31.7) 2 phantom limb non-thermal sensation (itch, shock, heavy) 7 36.8 No 13 (68.4) 1 2 Yes 6 (31.7) 2 2 phantom limb non-thermal sensation (position, shape, something that touches) 7 36.8 Yes 12 (63.2) 7 7 Soluti c phantom limb sen	NP	No Pain	
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Yes12 (63.2)7thantom limb no-movement sensation (position, hape, something that touches)8 (42.1)8lo8 (42.1)8ies11 (57.9)8bynamic phantom limb sensation (opens and closes he hand, rotates, or rocks the limb)7 (36.8)9lo7 (36.8)12 (63.2)7itatic phantom limb sensation (member stretched or exed)10 (52.6)1lo10 (52.6)1lo6 (31.6)7ies9 (47.3)5he phantom limb sensation moves involuntarily6lo6 (31.6)7ies13 (68.4)14idotaret / very much2 (10.6)14ittle / nothing13 (68.4)14lot applicable/ without answer4 (21.0)14			
hantom limb no-movement sensation (position, hape, something that touches) bo 8 (42.1) 8 es 11 (57.9) 8 ynamic phantom limb sensation (opens and closes he hand, rotates, or rocks the limb) bo 7 (36.8) 9 es 12 (63.2) 7 tatic phantom limb sensation (member stretched or exed) bo 10 (52.6) 1 es 9 (47.3) 5 he phantom limb sensation moves involuntarily bo 6 (31.6) 7 es 13 (68.4) 5 hantom limb sensation interference in habitual asks loderate / very much 2 (10.6) ittle / nothing 13 (68.4) 11 jot applicable/ without answer 4 (21.0)	9 (56.3)	3 (15.8)	0.512**
hape, something that touches)8io8 (42.1)8ies11 (57.9)8ynamic phantom limb sensation (opens and closes he hand, rotates, or rocks the limb)11 (57.9)8io7 (36.8)9ies12 (63.2)7tatic phantom limb sensation (member stretched or exed)10 (52.6)1ies9 (47.3)5he phantom limb sensation moves involuntarily631.6)7ies13 (68.4)14io6 (31.6)7isks13 (68.4)14idd applicable/ without answer4 (21.0)14	7 (43.7)	4 (17.4)	
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he hand, rotates, or rocks the limb) to 7 (36.8) 5 es 12 (63.2) 7 tatic phantom limb sensation (member stretched or exed) to 10 (52.6) 1 es 9 (47.3) 5 he phantom limb sensation moves involuntarily to 6 (31.6) 7 es 13 (68.4) 5 hantom limb sensation interference in habitual asks toderate / very much 2 (10.6) title / nothing 13 (68.4) 11 tot applicable/ without answer 4 (21.0)	8 (50.0)	2 (28.6)	
tatic phantom limb sensation (member stretched or exed) 12 (63.2) 7 io 10 (52.6) 1 es 9 (47.3) 5 he phantom limb sensation moves involuntarily 6 6 (31.6) 7 io 6 (31.6) 7 es 13 (68.4) 5 hantom limb sensation interference in habitual asks 13 (68.4) 10 loderate / very much 2 (10.6) 13 (68.4) 10 ittle / nothing 13 (68.4) 10 iot applicable/ without answer 4 (21.0) 5			
Allo 10 (52.6) 1 Yes 9 (47.3) 5 The phantom limb sensation moves involuntarily 1 Io 6 (31.6) 7 Yes 13 (68.4) 5 Yhantom limb sensation interference in habitual asks 3 Adderate / very much 2 (10.6) 1 Ittle / nothing 13 (68.4) 11 Iot applicable/ without answer 4 (21.0) 11	9 (56.3)	3 (42.9)	0.512*
Yes 9 (47.3) 5 Yhe phantom limb sensation moves involuntarily 6 (31.6) 7 Io 6 (31.6) 7 Yes 13 (68.4) 5 Yhantom limb sensation interference in habitual asks 3 Moderate / very much 2 (10.6) 11 ittle / nothing 13 (68.4) 11 Iot applicable/ without answer 4 (21.0) 11	7 (43.7)	4 (57.1)	
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he phantom limb sensation moves involuntarily o 6 (31.6) 7 es 13 (68.4) 9 hantom limb sensation interference in habitual asks loderate / very much 2 (10.6) ittle / nothing 13 (68.4) 10 ot applicable/ without answer 4 (21.0)	5 (31.3)	1 (14.3)	
loo 6 (31.6) 7 les 13 (68.4) 5 hantom limb sensation interference in habitual asks loderate / very much 2 (10.6) title / nothing 13 (68.4) 10 lot applicable/ without answer 4 (21.0)	(· · · /	,	
es 13 (68.4) 5 hantom limb sensation interference in habitual isks loderate / very much 2 (10.6) ittle / nothing 13 (68.4) 11 ot applicable/ without answer 4 (21.0)	7 (43.7)	3 (42.9)	0.731**
hantom limb sensation interference in habitual asks 2 (10.6) loderate / very much 2 (10.6) tittle / nothing 13 (68.4) 14 lot applicable/ without answer 4 (21.0) 14	9 (56.3)	4 (57.1)	
ttle / nothing13 (68.4)1ot applicable/ without answer4 (21.0)	- ()	. (2)	
ot applicable/ without answer 4 (21.0)	1 (6.2)	0 (0.0)	0.753**
	10 (62.5)	6 (85.7)	
otal 19 (100) 1	5 (6.3)	1 (14.3)	
2 test	16 (100)	7 (100)	

** Yates correction

PISPER International Society of Physical and Physical Society of Physical Society of Physical

Progression, rytmyn, ;icalization, and character of pain

Parameter	Feature	Ν	(%)
Followup	Stable	100	(86,2)
	Progressive	13	(11,2)
	Regressive	2	(1,7)
	Floating	1	(0,9)
	TOTAL	116	(100,0)
Rytmyn	Morning	2	(1,7)
	Night	13	(11,2)
	Daytime	99	(85,4)
	Morning and night	2	(1,7)
	TOTAL	116	(100,0)
Localization	Deep	108	(93,1)
	Superficial	4	(3,4)
	Supeficial and deep	4	(3,4)
	TOTAL	116	(100,0)
Character	Constant	83	(71,6)
	Paroxysmal	4	(3,5)
	Paroxysmal and constant	29	(25,0)
	TOTAL	116	(100,0)



MPQ pain descriptors Mean global score = 11.7 (>evaluative)

Sensitive	N	Affective	N	Evaluative	N	Miscelanea	N
Burning	80	Sickening	19	Intense	57	Cool	14
Flashing	58	Tiring	18	Umbearable	27	Thight	12
Tingling	34	Blinding	16	Troublesome	12	Drawing	8
Throbbing	31	Frightful	16	Miserable	6	Torturing	7
Jumping	29	Exausting	8	Annoying	6	Cold	6
Pricking	28	Fearful	8			Numb	5
Tugging	20	Grueling	8			Spreading	5
Heavy	17	Suffocating	7				
Pressing	14	Vicious	7		Phantom Limb	Pain 23 (18.8%) 40%	
Aching	12	Terrifying	5		Active	14 (60.9%)	
Pinching	12	Punishing	4		Static Sporadic	5 (21.7%) 4 (17.4%)	
Smarting	10	Wretched	4		Dominant	14 (60.9%)	
Crushing	9	Punshing	4		Non-dominant	9 (39.1%)	

N=116

Number of NPSI descriptors higher in mixed pain / neuropathic pain patients

Roots avulsion diagnoses, n (%)				0.695
1 or 2 roots	8 (36.3)	9 (41)	5 (22.7)	
3 roots	2 (18.2)	5 (45.4)	4 (36.4)	
4 or 5 roots	9 (39.2)	10 (43.4)	4 (17.4)	
Total	19 (100)	24 (100)	13 (100)	

Table 3S. Distribution of pain according to injury characteristics among patients with BPA

Variable	Pain			No Pain		otal	p *
	n	%	n	%	n	%	_
Lesion cause							
Motocycle accident	28	75,7	9	24,3	37	100	0,952**
Others	15	78,9	4	21,1	19	100	
Main cause of annoyance							
Pain with or without lack of movement	40	97,6	1	2,4	41	100	<0,001**
Others	3	20	12	80	15	100	
Total	43	76,8	13	23,2	56	100	

NPSI - Descriptives	NP	MP	No Pain	р	M x NP <i>p</i> **	M x NoP <i>p</i> **	NP x NoP
Burning	4,89 ± 3,68	6,92 ± 2,86	0.46 ± 1.20	< 0.001	0.616	< 0.001	0.002
Squeezing	3,79 ± 3,91	5,33 ± 3,87	0.00 ± 0.00	< 0.001	0.424	< 0.001	0.003
Pressure	3,63 ± 3,89	4,88 ± 3,62	0.15 ± 0.55	< 0.001	0.472	< 0.001	0.017
Electric Shocks	4,84 ± 4,13	5,50 ± 3,01	0.61 ± 2.22	< 0.001	0.940	< 0.001	0.009
Stabbing	3,79 ± 4,24	4,50 ± 3,67	0.00 ± 0.00	0.001	0.780	< 0.001	0.013
Provoked by brushing	1,68 ± 3,06	4,42 ± 4,06	0.15 ± 0.55	0.001	0.059	0.003	0.216
Provoked by pressure	1,74 ± 3,30	5,17 ± 3,64	0.15 ± 0.55	< 0.001	0.008	< 0.001	0.322
Provoked by contact with cold	2,68 ± 4,03	5,38 ± 3,74	0.00 ± 0.00	< 0.001	0.094	< 0.001	0.042
Pins and needles	3,21 ± 4,17	4,58 ± 4,03	0.61 ± 2.22	0.012	0.556	0.007	0.099
Tingling	5,21 ± 4,24	4,75 ± 3,85	1.46 ± 3.23	0.025	0.785	0.042	0.036

BPI, DN4, and NPSI scores higher in mixed pain patients

BPI - funcional InterefenceNPMPNo Pain p^* p^{**} p^{**} Neuropathic PainGeneral activity 5.00 ± 3.20 7.50 ± 2.41 0.73 ± 2.41 <0.001 0.032 <0.001 0.005 Mood 5.63 ± 3.32 6.08 ± 3.40 0.45 ± 1.51 <0.001 0.908 <0.001 <0.001 walking ability 4.42 ± 3.78 6.46 ± 3.45 1.18 ± 3.06 0.002 0.180 0.004 0.044 Normal work 6.11 ± 4.57 7.96 ± 3.21 0.73 ± 2.41 <0.001 0.452 <0.001 0.005 Relation with other people 4.16 ± 3.95 5.92 ± 3.57 1.36 ± 3.04 0.005 0.272 0.004 0.131 Sleep 5.79 ± 3.99 7.92 ± 2.65 0.00 ± 0.001 0.167 <0.001 <0.029 Enjoyment of life 4.53 ± 3.56 5.46 ± 3.81 1.18 ± 2.71 0.009 0.643 0.010 0.029	Characterization of pain syndromes in patients with brachial plexus avulsion, n (%)	NP 19 (33.9)	MP 24 (42.9)	No Pain 13 (23.2)	p*	MP x NP <i>p</i> **	MP x NoP p**	NP x NoP <i>p</i> **	_
BPI pain interference (0-10) 5.09 ± 2.80 6.75 ± 2.42 1.19 ± 3.02 <0.001 <1.01 <0.001 <0.001 DN4 score (0-10) 5.74 ± 1.69 7.21 ± 1.25 3.15 ± 1.77 <0.001	BPI pain VAS (0–100)	69.8 ± 28.9	72.6 ± 23.7	0.92 ± 2.78	<0.001	0.928	< 0.001	< 0.001	
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	BPI pain intensity (0–10)	6.21 ± 1.75	6.46 ± 1.47	0.53 ± 1.45	<0.001	0.942	< 0.001	< 0.001	
No-neuropathic pain, DN4 < 4, n (%) 2 (11.8) 0 (0) 9 (69.2) Neuropathic pain, DN4 > 4, n (%) 17 (88.2) 24 (100) 4 (30.8) Quality of neuropathic pain (NPSI) Continuous ongoing superficial pain (pressure/squeezing), Intensity (0–10) 4.89 ± 3.68 6.92 ± 2.86 0.46 ± 1.20 <0.001 0.161 <0.001 0.002 Continuous ongoing deep pain (pressure/squeezing), Intensity (0–10) 4.32 ± 3.71 5.00 ± 2.53 0.30 ± 1.11 <0.001 0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.002 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 $<0.$	BPI pain interference (0–10)	5.09 ± 2.80	6.75 ± 2.42	1.19 ± 3.02	<0.001	0.174	< 0.001	< 0.001	_
Neuropathic pain, DN4 > 4, n (%) 17 (88.2) 24 (100) 4 (30.8) Quality of neuropathic pain (NPSI) Continuous ongoing superficial pain (burning), Intensity (0–10) 4.89 ± 3.68 6.92 ± 2.86 0.46 ± 1.20 <0.001	DN4 score (0–10)	5.74 ± 1.69	7.21 ± 1.25	3.15 ± 1.77	<0.001	0.008	< 0.001	0.002	
Quality of neuropathic pain (NPSI) Continuous ongoing superficial pain (burning), Intensity (0–10) 4.89 ± 3.68 6.92 ± 2.86 0.46 ± 1.20 <0.001 0.161 <0.001 0.002 Continuous ongoing geep pain (pressure/squeezing), Intensity (0–10) 3.71 ± 3.46 5.10 ± 3.32 0.07 ± 0.27 <0.001 0.340 <0.001 <0.001 Evoked pain (allodynia to brush, cold and pressure), Intensity (0–10) 4.32 ± 3.71 5.00 ± 2.53 0.30 ± 1.11 <0.001 0.002 0.001 Paraxesthesia (Lingling, pins and needles), Intensity (0–10) 2.04 ± 2.47 4.99 ± 3.05 0.010 ± 0.37 <0.001 0.002 0.008 NPSI- total score (0–100) 3.55 ± 2.02 5.14 ± 2.04 0.36 ± 0.54 <0.001 <0.001 <0.001 Affective (0–5) 0.71 ± 0.25 0.81 ± 0.18 0.14 ± 0.25 <0.001 <0.001 <0.001 Evaluative (0–2) 0.73 ± 0.25 0.19 ± 0.33 <0.001 0.001 <0.001 <0.001 Mood 5.63 ± 3.32 0.50 ± 3.41 0.73 ± 2.41 <0.001 0.002 <0.001 <0.001 Isues focused on the pain lisue focused on the pain l	No-neuropathic pain, DN4 < 4, n (%)	2 (11.8)	0 (0)	9 (69.2)					
Continuous ongoing superficial pain (burning), Intensity (0–10) 4.89 ± 3.68 6.92 ± 2.86 0.46 ± 1.20 <0.001	Neuropathic pain, DN4 > 4, n (%)	17 (88.2)	24 (100)	4 (30.8)					_
Continuous ongoing deep pain (pressure/squeezing), Intensity (0–10) 3.71 ± 3.46 5.10 ± 3.32 0.07 ± 0.27 <0.001	Quality of neuropathic pain (NPSI)								
Evoked pain (allodynia to brush, cold and pressure), Intensity (0-10) 4.32 ± 3.71 5.00 ± 2.53 0.30 ± 1.11 <0.001 0.742 <0.001 0.003 Paroxysmal pain (electric shocks/stabbing), Intensity (0-10) 2.04 ± 2.47 4.99 ± 3.05 0.10 ± 0.37 <0.001 0.007 <0.001 0.009 Paraesthesia/Dysaesthesia (tingling, pins and needles), Intensity (0-10) 4.21 ± 3.08 4.67 ± 2.85 1.04 ± 1.83 0.002 0.986 0.002 0.008 NPSI- total score (0-100) 3.55 ± 2.02 5.14 ± 2.04 0.36 ± 0.54 <0.001 0.036 <0.001 <0.001 Affective (0-5) 0.76 ± 0.29 0.73 ± 0.30 0.06 ± 0.15 <0.001 0.918 <0.001 <0.001 Evaluative (0-2) 0.86 ± 0.23 0.79 ± 0.25 0.19 ± 0.33 <0.001 0.926 <0.001 <0.001 Total score (0-15) 11.40 ± 3.20 12.00 ± 2.68 1.77 ± 3.00 <0.001 0.002 <0.001 <0.001 BPI - functional IntereferceNPMPNo Pain p^* p^{**} p^{**} p^{**} p^{**} General activity 5.00 ± 3.20 7.50 ± 3.21 0.73 ± 2.41 <0.001 0.908 <0.001 <0.001 Nordwalking ability 4.42 ± 3.78 6.46 ± 3.45 1.18 ± 3.06 0.002 <0.001 0.004 0.004 Moodtotal score 5.79 ± 3.99 7.92 ± 2.65 0.001 ± 0.005 0.001 0.001 0.002 Normal work 6.11 ± 4.57	Continuous ongoing superficial pain (burning), Intensity (0–10)	4.89 ± 3.68	6.92 ± 2.86	0.46 ± 1.20	<0.001	0.161	< 0.001	0.002	
Paroxysmal pain (electric shocks/stabbing), Intensity (0–10) 2.04 ± 2.47 4.99 ± 3.05 0.10 ± 0.37 < 0.001 0.007 < 0.001 0.009 Paraesthesia/Dysaesthesia (tingling, pins and needles), Intensity (0–10) 4.21 ± 3.08 4.67 ± 2.85 1.04 ± 1.83 0.002 0.986 0.002 0.008 NPSI- total score (0–100) 3.55 ± 2.02 5.14 ± 2.04 0.36 ± 0.54 < 0.001 < 0.001 < 0.001 Brief-MPQ, Sensory (0–8) 0.71 ± 0.25 0.81 ± 0.18 0.14 ± 0.25 < 0.001 < 0.001 < 0.001 Affective (0–5) 0.76 ± 0.29 0.73 ± 0.30 0.66 ± 0.15 < 0.001 < 0.001 < 0.001 BPI - functional interferec NP MP No Pain p^* p^{**}	Continuous ongoing deep pain (pressure/squeezing), Intensity (0–10)	3.71 ± 3.46	5.10 ± 3.32	0.07 ± 0.27	<0.001	0.340	< 0.001	< 0.001	
Paraesthesia/Dysaesthesia (tingling, pins and needles), Intensity (0–10) 4.21 ± 3.08 4.67 ± 2.85 1.04 ± 1.83 0.002 0.986 0.002 0.008 NPSI- total score (0–100) 3.55 ± 2.02 5.14 ± 2.04 0.36 ± 0.54 <0.001 <0.001 <0.001 Brief-MPQ, Sensory (0–8) 0.71 ± 0.25 0.81 ± 0.18 0.14 ± 0.25 <0.001 <0.001 <0.001 Affective (0–5) 0.76 ± 0.29 0.73 ± 0.30 0.06 ± 0.15 <0.001 <0.001 <0.001 Evaluative (0–2) 0.86 ± 0.23 0.79 ± 0.25 0.19 ± 0.33 <0.001 <0.001 <0.001 Total score (0–15) 11.40 ± 3.20 12.00 ± 2.68 1.77 ± 3.00 <0.001 <0.001 <0.001 General activity 5.00 ± 3.20 7.50 ± 2.41 0.73 ± 2.41 <0.001 0.002 <0.001 <0.001 Mood 5.63 ± 3.32 6.08 ± 3.40 0.45 ± 1.51 <0.001 0.004 0.004 <0.001 walking ability 4.42 ± 3.78 6.46 ± 3.45 1.18 ± 3.06 0.002 0.001 <0.001 Normal work 6.11 ± 4.57 7.96 ± 3.21 0.73 ± 2.41 <0.001 0.452 <0.001 0.005 Sleep 5.79 ± 3.99 7.92 ± 2.65 0.001 ± 0.004 0.167 <0.001 $sues focused on the pGeneral of life4.53 \pm 3.565.46 \pm 3.811.18 \pm 2.710.0000.6430.0010.025Normal work6.11 \pm 4.577.92 \pm 2.650.001 \pm 0.026$	Evoked pain (allodynia to brush, cold and pressure), Intensity (0–10)	4.32 ± 3.71	5.00 ± 2.53	0.30 ± 1.11	<0.001	0.742	< 0.001	0.003	
NPSI- total score $(0-100)$ 3.55 ± 2.02 5.14 ± 2.04 0.36 ± 0.54 <0.001 0.036 <0.001 <0.001 Brief-MPQ, Sensory $(0-8)$ 0.71 ± 0.25 0.81 ± 0.18 0.14 ± 0.25 <0.001 0.414 <0.001 <0.001 Affective $(0-5)$ 0.76 ± 0.29 0.73 ± 0.30 0.06 ± 0.15 <0.001 0.918 <0.001 <0.001 Evaluative $(0-2)$ 0.86 ± 0.23 0.79 ± 0.25 0.19 ± 0.33 <0.001 0.926 <0.001 <0.001 Total score $(0-15)$ 11.40 ± 3.20 12.00 ± 2.68 1.77 ± 3.00 <0.001 0.926 <0.001 <0.001 Neuropathic Pain General activity 5.00 ± 3.20 7.50 ± 2.41 0.73 ± 2.41 <0.001 0.002 <0.001 Neuropathic Pain Mood 5.63 ± 3.32 6.08 ± 3.40 0.45 ± 1.51 <0.001 0.004 0.004 0.004 0.004 0.004 0.004 0.004 0.004 0.004 0.004 0.004 0.004 0.004 0.004 0.004 0.004 0.004 0.004	Paroxysmal pain (electric shocks/stabbing), Intensity (0–10)	2.04 ± 2.47	4.99 ± 3.05	0.10 ± 0.37	<0.001	0.007	< 0.001	0.009	
Brief-MPQ, Sensory (0-8) 0.71 ± 0.25 0.81 ± 0.18 0.14 ± 0.25 <0.001 <0.001 <0.001 Affective (0-5) 0.76 ± 0.29 0.73 ± 0.30 0.06 ± 0.15 <0.001 0.918 <0.001 <0.001 Evaluative (0-2) 0.86 ± 0.23 0.79 ± 0.25 0.19 ± 0.33 <0.001 0.629 <0.001 <0.001 Total score (0-15) 11.40 ± 3.20 12.00 ± 2.68 1.77 ± 3.00 <0.001 0.926 <0.001 <0.001 BPI - funcional InterfenceNPMPNo Pain p^* p^{**} p^{**} BPI Functional interfenceGeneral activity 5.00 ± 3.20 7.50 ± 2.41 0.73 ± 2.41 <0.001 0.908 <0.001 <0.001 Mood 5.63 ± 3.32 6.08 ± 3.40 0.45 ± 1.51 <0.001 0.908 <0.001 <0.001 walking ability 4.42 ± 3.78 6.46 ± 3.45 1.18 ± 3.06 0.002 0.180 0.004 0.044 Normal work 6.11 ± 4.57 7.96 ± 3.21 0.73 ± 2.41 <0.001 0.452 <0.001 0.005 Relation with other people 5.92 ± 3.57 1.36 ± 3.04 0.005 0.272 0.004 0.131 Issues focused on the pSleep 5.79 ± 3.99 7.92 ± 2.65 0.00 ± 0.001 0.643 0.010 0.029 Enjoyment of life 4.53 ± 3.56 5.46 ± 3.81 1.18 ± 2.71 0.000 0.643 0.010 0.029	Paraesthesia/Dysaesthesia (tingling, pins and needles), Intensity (0–10)	4.21 ± 3.08	4.67 ± 2.85	1.04 ± 1.83	0.002	0.986	0.002	0.008	
Affective (0-5) 0.76 ± 0.29 0.73 ± 0.30 0.06 ± 0.15 <0.001 0.918 <0.001 <0.001 <0.001 Evaluative (0-2) 0.86 ± 0.23 0.79 ± 0.25 0.19 ± 0.33 <0.001 0.629 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.0	NPSI- total score (0–100)	3.55 ± 2.02	5.14 ± 2.04	0.36 ± 0.54	<0.001	0.036	< 0.001	< 0.001	_
Evaluative (0-2) 0.86 ± 0.23 0.79 ± 0.25 0.19 ± 0.33 <0.001 0.629 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001	Brief-MPQ, Sensory (0–8)	0.71 ± 0.25	0.81 ± 0.18	0.14 ±0.25	<0.001	0.414	< 0.001	< 0.001	
Total score (0-15) 11.40 ± 3.20 12.00 ± 2.68 1.77 ± 3.00 <0.001 0.926 <0.001 <0.001 <0.001 BPI Functional interferBPI - funcional InterefenceNPMPNo Pain p^* p^{**} p^{**} p^{**} p^{**} BPI Functional interferGeneral activity 5.00 ± 3.20 7.50 ± 2.41 0.73 ± 2.41 <0.001 0.032 <0.001 0.005 $sues$ focused on the pMood 5.63 ± 3.32 6.08 ± 3.40 0.45 ± 1.51 <0.001 0.908 <0.001 <0.001 $sues$ focused on the pwalking ability 4.42 ± 3.78 6.46 ± 3.45 1.18 ± 3.06 0.002 0.180 0.004 0.044 $with other people, appression of the people, appression of the peoplethe lifeNormal work6.11 \pm 4.577.96 \pm 3.210.73 \pm 2.41<0.0010.452<0.0010.005Mixed PainSleep5.79 \pm 3.997.92 \pm 2.650.00 \pm 0.00<0.0010.167<0.001<0.029Sleep5.79 \pm 3.997.92 \pm 2.650.00 \pm 0.00<0.001<0.029<0.021<0.021<0.021Tuble4.53 \pm 3.565.46 \pm 3.811.18 \pm 2.710.0090.6430.001<0.029Comparison of life4.53 \pm 3.665.46 \pm 3.811.18 \pm 2.710.0090.6430.001<0.029$	Affective (0–5)	0.76 ± 0.29	0.73 ± 0.30	0.06 ±0.15	<0.001	0.918	< 0.001	< 0.001	
BPI - funcional InterefenceNPMPNo Pain p^* p^{**} p^{**} p^{**} No Pain p^{**} Neuropathic PainGeneral activity 5.00 ± 3.20 7.50 ± 2.41 0.73 ± 2.41 <0.001 0.032 <0.001 0.005 Mood 5.63 ± 3.32 6.08 ± 3.40 0.45 ± 1.51 <0.001 0.908 <0.001 <0.001 Walking ability 4.42 ± 3.78 6.46 ± 3.45 1.18 ± 3.06 0.002 0.180 0.004 0.044 Normal work 6.11 ± 4.57 7.96 ± 3.21 0.73 ± 2.41 <0.001 0.452 <0.001 0.005 Relation with other people 4.16 ± 3.95 5.92 ± 3.57 1.36 ± 3.04 0.005 0.272 0.004 0.131 Sleep 5.79 ± 3.99 7.92 ± 2.65 0.00 ± 0.00 <0.001 0.167 <0.001 0.029 Enjoyment of life 4.53 ± 3.56 5.46 ± 3.81 1.18 ± 2.71 0.009 0.643 0.010 0.029	Evaluative (0–2)	0.86 ± 0.23	0.79 ± 0.25	0.19 ±0.33	<0.001	0.629	< 0.001	< 0.001	
BPI - funcional InterefenceNPMPNo Pain p^* p^{**} $p^$	Total score (0–15)	11.40 ± 3.20	12.00 ± 2.68	1.77 ± 3.00	<0.001	0.926	< 0.001	< 0.001	BPI Functional interference
General activity 5.00 ± 3.20 7.50 ± 2.41 0.73 ± 2.41 < 0.001 0.032 < 0.001 0.005 ability to walk, relationshMood 5.63 ± 3.32 6.08 ± 3.40 0.45 ± 1.51 < 0.001 0.908 < 0.001 < 0.001 with other people, appressionwalking ability 4.42 ± 3.78 6.46 ± 3.45 1.18 ± 3.06 0.002 0.180 0.004 0.044 with other people, appressionNormal work 6.11 ± 4.57 7.96 ± 3.21 0.73 ± 2.41 < 0.001 0.452 < 0.001 0.005 the lifeRelation with other people 4.16 ± 3.95 5.92 ± 3.57 1.36 ± 3.04 0.005 0.272 0.004 0.131 Issues focused on the pSleep 5.79 ± 3.99 7.92 ± 2.65 0.00 ± 0.00 < 0.001 0.167 < 0.001 < 0.001 $General activity, work and activity,$	BPI - funcional Interefence	NP	MP	No Pain	p*				Neuropathic Pain
Mood 5.63 ± 3.32 6.08 ± 3.40 0.45 ± 1.51 < 0.001 0.908 < 0.001 < 0.001 with other people, apprendictwalking ability 4.42 ± 3.78 6.46 ± 3.45 1.18 ± 3.06 0.002 0.180 0.004 0.044 with other people, apprendictNormal work 6.11 ± 4.57 7.96 ± 3.21 0.73 ± 2.41 < 0.001 0.452 < 0.001 0.005 0.005 Relation with other people 4.16 ± 3.95 5.92 ± 3.57 1.36 ± 3.04 0.005 0.272 0.004 0.131 Issues focused on the people dent of lifeSleep 5.79 ± 3.99 7.92 ± 2.65 0.00 ± 0.00 < 0.001 0.167 < 0.001 < 0.001 Enjoyment of life 4.53 ± 3.56 5.46 ± 3.81 1.18 ± 2.71 0.009 0.643 0.010 0.029 Table 2 5.92 ± 0.202 0.73 ± 0.402 0.238 ± 0.023 0.024 0.240 0.240 0.240	General activity	5.00 ± 3.20	7.50 ± 2.41	0.73 ± 2.41	< 0.	001 0.03	2 < 0.001	0.005	
walking ability 4.42 ± 3.78 6.46 ± 3.45 1.18 ± 3.06 0.002 0.180 0.004 0.044 the lifeNormal work 6.11 ± 4.57 7.96 ± 3.21 0.73 ± 2.41 < 0.001 0.452 < 0.001 0.005 $Mixed Pain$ Relation with other people 4.16 ± 3.95 5.92 ± 3.57 1.36 ± 3.04 0.005 0.272 0.004 0.131 Issues focused on the pSleep 5.79 ± 3.99 7.92 ± 2.65 0.00 ± 0.00 < 0.001 0.167 < 0.001 < 0.001 Enjoyment of life 4.53 ± 3.56 5.46 ± 3.81 1.18 ± 2.71 0.009 0.643 0.010 0.029 Table 2006 5.02 ± 0.02 0.73 ± 0.420 0.232 ± 0.021 0.242 10.024 10.024	Mood	5.63 ± 3.32	6.08 ± 3.40	0.45 ± 1.51	< 0.	001 0.90	8 < 0.001	< 0.001	with other people, appreciation
Relation with other people 4.16 ± 3.95 5.92 ± 3.57 1.36 ± 3.04 0.005 0.272 0.004 0.131 Issues focused on the pSleep 5.79 ± 3.99 7.92 ± 2.65 0.00 ± 0.00 < 0.001 0.167 < 0.001 < 0.001 < 0.001 General activity, work and the pEnjoyment of life 4.53 ± 3.56 5.46 ± 3.81 1.18 ± 2.71 0.009 0.643 0.010 0.029	walking ability	4.42 ± 3.78	6.46 ± 3.45	1.18 ± 3.06	6 0.	002 0.18	0 0.004	0.044	
Sleep 5.79 ± 3.99 7.92 ± 2.65 0.00 ± 0.00 < 0.001 0.167 < 0.001 < 0.001 General activity, work at the property of the p	Normal work	6.11 ± 4.57	7.96 ± 3.21	0.73 ± 2.41	< 0.	001 0.45	2 < 0.001	0.005	
Sieep 5.79 ± 3.99 7.32 ± 2.03 6.60 ± 6.001 6.107 € 0.001 € 0.001 Enjoyment of life 4.53 ± 3.56 5.46 ± 3.81 1.18 ± 2.71 0.009 0.643 0.010 0.029	Relation with other people	4.16 ± 3.95	5.92 ± 3.57	1.36 ± 3.04	ł 0.	005 0.27	2 0.004	0.131	Issues focused on the physic:
	Sleep	5.79 ± 3.99	7.92 ± 2.65	0.00 ± 0.00) < <u>0</u> .	001 0.16	7 < 0.001	< 0.001	General activity, work and sleep
Total Score $5.09 + 2.80 + 2.80 + 2.42 + 0.38 \pm 0.93 < 0.001 + 0.942 < 0.001 < 0.001 + 0.001 = 0.001 $	Enjoyment of life	4.53 ± 3.56	5.46 ± 3.81	1.18 ± 2.71	0.	009 0.64	3 0.010	0.029	
	Total Score	5.09 ± 2.80	6.76 ± 2.42	0.38 ± 0.93	· < 0.	001 0.94	2 < 0.001	< 0.001	

leuropathic Pain ssues focused on the psychic: bility to walk, relationship ith other people, appreciation of



QoL SF-12 physical domain worse in mixed pain patients

Table 7S. Descriptive statistics (mean ± SD) of the presence of pain according to characteristics of functionality, quality of life and health in patients with BPA.

Psychological aspects	NP	MP	No Pain	p *	M x NP <i>p</i> **	M x NoP <i>p</i> **	NP x NoP <i>p</i> **
HADS	·		·		·		
Anxiety (0–21)	7.00 ± 5.43	8.46 ± 4.16	1.15 ± 1.95	<0,001	0.605	<0.001	0.001
Depression (0–21)	5.42 ± 4.76	6.88 ± 3.96	1.38 ± 2.84	<0,001	0.437	<0.001	0.009
Pain catastrophizing scale							
Rumination (0–5)	2.83 ± 1.97	2.58 ± 1.57	0.31 ± 0.99	<0,001	0.882	<0.001	0.002
Helplessness (0–5)	2.08 ± 1.65	2.69 ± 1.30	0.23 ± 0.45	<0,001	0.304	<0.001	0.004
Total (0–5)	2.46 ± 1.61	2.64 ± 1.31	$0,27 \pm 0.70$	<0,001	0.899	<0.001	0.002
Quality of life and disability							
SF-12							
PCS (0-100)	38.6 ± 9.70	31.2 ± 7.50	51.2 ± 7.40	<0,001	0.044	<0.001	0.003
MCS (0–100)	45.9 ± 13.6	47.0 ± 13.7	54.6 ± 9.52	0.173	0.899	0.393	0.118
Quick Dash score (0–100)	61.5 ± 22.0	66.2 ± 13.5	21.3 ± 16.6	<0,001	0.919	<0.001	<0.001

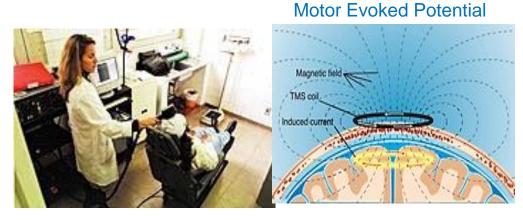
* Kuskal-wallis with **Dwass-Steel-Critchlow-Fligner pairwise comparisons Abbreviations: MP, mixed pain; NP, neurophatic pain; NoP, no pain; HADS: Hospital Anxiety Depression Symptoms; SE-12: Health survey: 12-item questionnaire: PCS: physical component: MCS: mental component



Cortical Excitability

•Contralateral motor cortex TMS induced paresthesias in the affected limb

•Surface area: 2.1 - 42.8 ²cm (mean=10.6 cm²; SD=11.11; median=²6.1 cm)

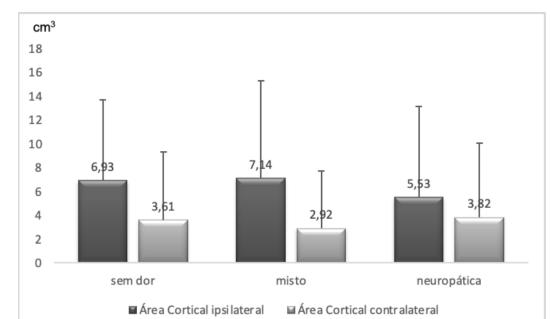


Motor threshhold	Pos	itive	Ne	gative		Total
	Ν	(%)	N	(%)	N	(%)
41 a 50	0	(0,0)	2	(100,0)	2	(5,7)
51 a 60	6	(50,0)	6	(50,0)	12	(34,3)
61 a 70	4	(36,4)	7	(63,6)	11	(31,4)
71 a 80	4	(50,0)	4	(50,0)	8	(22,9)
81 a 90	0	(0,0)	2	(100,0)	2	(5,7)
Total	14	(40,0)	21	(60,0)	35	(100,0)



- Mixed pain: variation 4.22²cm
- Pain-free group: variation 3.32²cm
- Neuropathic pain: variation 1.71²cm

Gráfico 27. Média das Áreas Corticais (cm3) do cortex motor primário segundo as áreas avaliadas e dor entre os doentes com APB.





Cortical Excitability

Motor Evoked Potential, Intracortical Inhibition, Resinting Motor Potential, Intracortical Facilitation

Tipo		L	.MR			PEM 120					PEM 140				
	ipsilateral	contra lateral	trapézio	р*	p**	ipsilateral	contra lateral	trapézio	p*	p**	ipsilateral	contra lateral	trapézio	р*	p**
sem dor	[48; 40-52]	[46; 39-61]	[48,5; 45-57]	0,367ª	0,812ª	[228; 22,3-719]	[80,4; 27,2-430]	[53,5; 26,7-129]	0,588	0,380	[947; 48-1570]	[335; 68-934]	[113; 46-181]	0,455	0,380
com dor	[50; 43-58]	[30; 0-57]	[54; 48-63]	<0 ,001ª	<0 ,001ª	[183; 66,9-487]	[11,2; 0-217]	[93,2; 32,2-170]	0,003	0,725	[438; 173-967]	[10; 0-520]	[172; 60,5-399]	0,024ª	0,735
misto	[50; 43,5-58]	[19; 0-54]	[55; 48-64]	0,002ª	<0,001	[193; 72-515]	[5,6; 0-340]	[85,3; 39,3-167]	0,037	0,922	[710; 180-1525]	[5; 0-1500]	[241; 62,8-391]	0,060	0,833
neuropático	[50; 43-55]	[30; 0-60]	[53; 48,5-61,5]	0,097	0,033	[144;55,9-372]	[21,9; 0-156]	[142; 24,7-172]	0,064	0,489	[275; 144-587]	[26,3; 0-463]	[126; 52,9-404]	0,313ª	0,934

Tine de Der	Inibição Intracortical									
Tipo de Dor	ipsilateral	contralateral	trapézio	p*	p**	ipsilateral	contralateral	trapézio	p*	p **
sem dor	[403; 32,5-479]	[121; 46,1-178]	[79,9; 35-120]	0,033	0,677	[652; 44,9-944]	[320; 124-429]	[99,7; 46-135]	0,244	0,077
com dor	[140; 39-283]	[0; 0-150]	[85,5; 25,8-210]	0,023	0,831	[226; 103-879]	[0; 0-393]	[140; 47,4-287]	<0 ,001	0,756
misto	[143; 59,3-310]	[12; 0-220]	[96,5; 42,9-240]	0,136	0,643	[244; 102-1186]	[7,6; 0-694]	[135; 84,8-322]	0,021	0,684
neuropático	[126; 35,4-283]	[0; 0-144]	[76,1; 15,7-140]	0,057	0,890	[194; 109-601]	[0; 0-192]	[140; 22,1-214]	0,007	0,978

Contralateral hemisphere:

 \downarrow MEP120% (p = 0.003), MEP140% (p = 0.024) and RMT (p < 0.001) ICF (p < 0.001). **Mixed pain**: MRI (p = 0.002), MEP 120% (p = 0.037), ICF (p = 0.021), statistical trend of MEP 140% (p = 0.060). **Neuropathic pain**: ICF (p = 0.007), trend MEP120% (p = 0.064), RMTL (p = 0.097) and ICI (p = 0.057)



Workup

Acute phase of traumatic brachial plexopathy

- Accuracy of the diagnosis in acute phase difficult: anatomy of the plexus, incomplete and complex lesions and injuries
- Diagnosis and estimation the severity of the lesion > prognostic, surgical, and rehabilitative purposes
- Electrodiagnosis: a mainstay in the diagnostic evaluation after the 3rd week
- Radiographies, computed tomography (bones and othe lesions), magnetic resonance imaging (peripheral nerve structures):

other soft-tissue or bone injuries

Management of traumatic brachial plexopathy

- Goals: preservation of the range of motion (ROM), improve strength, and management of pain
- Surgery: persistence of symptoms and signs despite appropriate conservative treatment
- Reparable injuries: primary reconstruction and debridement and decompression of the nerve issue
- Non-reparable injuries: neurotization or nerve transfers, spinal cord implantation of avulsed spinal nerves Carlstedt et al. 1995

LS P R M International Society of Physical

Birth-related brachial plexus palsy

- Controversies regarding surgical timing
- Small number of patients require surgical management
- Direct nerve transfers may minimize interpositional grafting procedures

Adult brachial plexus closed injury

- Evaluation of the situation, managing of pain, and starting rehabilitation.
- Advances
 - -Diagnostic imaging, electrophysiologics tests
 - Physical therapy and rehabilitation: multidisciplinary approach: improves symptoms and function in children and those with a stretch
 - type injury/outcome poorer in patients with root avulsions
- Acutely: traumatic mass effect ► prevention of irreversible atrophy of denervated muscles
- Functional restoration: microsurgical early exploration, neurolysis, nerve repair, nerve transfer, nerve grafting, neurotization, free muscle and tendon transfers, nerve rootlet reimplantation,

-Continuity of the nerve fascicles: conservative management

-Preganglionic brachial plexopathy and severe loss of function / multilevel root avulsions not amenable to direct repair: nerve

transfer ► restauration of biceps function (C6) and shoulder mobility (C5)

-Post-ganglionic with damaged fascicles: nerve decompression, nerve grafting, excising the damaged plexus segment + nerve auto-

graft with sural, phrenic, spinal accessory, or medial pectoral nerves

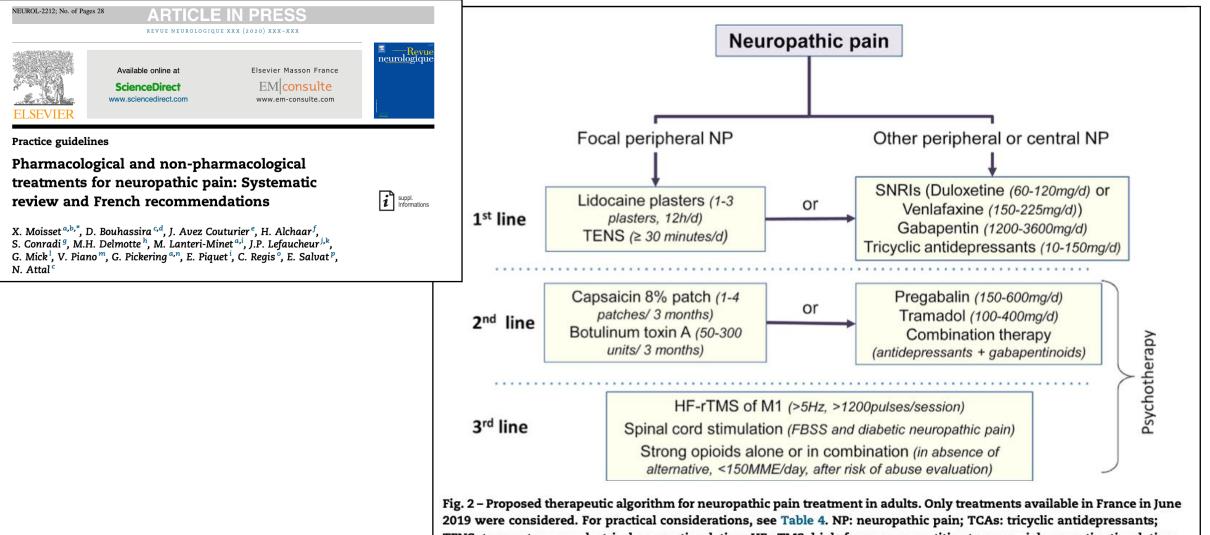


No consensus on the analgesic management Tricyclic antidepressants (amitryptiline) and or antiepileptic drugs

Empirical drug therapy

- Simple analgesics and NSAIDs: no help in the chronic phase
- TADs or serotonin and noradrenaline reuptake inhibitors (SNRIs)
- ADs + anti-epileptic agents (gabapentin, pregabalin, topiramate, carbamazepine, oxcarbazepine lamotrigine)
- Topicals: 5% lidocaine (lignocaine) patches, 8% capsaicine ?
- Opioids: tramadol, tapentadol, morphine, oxycodone, methadone, TD buprenorphine
- Botulinum toxin: post-ganglionic lesion
- Other drugs: cannabinoids, ketamine, clonidine, nefopam, coxibs, pamycin, intrathecal Trichostatin, IV immunoglobulin?
- Electroacupuncture
- Transcutaneous electrical nerve stimulation (TENS)
- Stellate ganglion blocks: CRPS





TENS: transcutaneous electrical nerve stimulation; HF-rTMS: high-frequency repetitive transcranial magnetic stimulation; M1: primary motor cortex; BTX-A: botulinum toxin type A; FBSS: failed back surgery syndrome; MME: mg morphine equivalent.

Surgery

Restaurative surgery

-Brachial plexus injury repair with direct suture, grafts or nerve transfers, minimizes the incidence and severity of neuropathic pain??? -Sooner the repair/ better the result *Berman et al. 1996*

Continuous pain: neuromodulation

Post-ganglionic lesion: peripheral nerve stimulation: 50–83% ▶ pain relief: 65–80% of the patients
 Cervical spinal cord stimulation: brachial plexus injuries effective in is 50%, failed previous DREZotomy?

-Pulsed radiofrequency: plexular lesion without avulsion?

-Thalamic and periaqueductal grey matter deep brain stimulation: 55% improvement in BPI and post-amputation pains



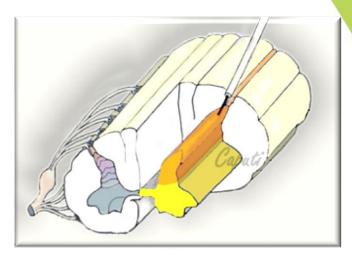


?

Dorsal entry zone region lesions

			Degree of pain relief at final follow-up (%)						
Lesioning method	Reference	No. of BPA patients	75% to 100%	50% to 75%	25% to 50%	<25%			
MDT	Jeanmonod and Sindou, 1991 ⁴	7 3	67%	0%	33%	0%			
MDT	Emery et al, 1997 ⁸	37	65%		27%	8%			
MDT	Guenot et al, 2003 ²	9	44%	22%	11%	22%			
MDT	Sindou et al, 2005 ⁷	55	38%	31%	31%	0%			
MDT ^a	Prestor, 2006 ¹³	26	76% (12% "con	nplete")	24%				
MDT	Zheng et al, 2009 ⁴⁵	14	64%		36%				
MDT	Aichaoui et al, 2011 ⁴	29	59%	24%	7%	10%			
MDT	Dong et al, 2012 ⁴⁹	7	100%	0%	0%	0%			
RF	Nashold and Ostdahl, 1979 ¹⁵	18	56%		17%	28%			
RF	Thomas and Sheehy, 198353	19	52%		32%	16%			
RF	Richter and Seitz, 1984 ⁵⁴	7	71%	0%	0%	29%			
RF	Samii and Moringlane, 1984 ¹⁶	22	77% ^c		14% ^c	9%			
RF	Thomas and Jones, 1984 ⁵⁵	34	59%		26%	15%			
RF ^b	Bruxelle et al, 1988 ¹⁹	18	83%	17%	0%	0%			
RF	Campbell et al, 1988 ⁶⁰	10	80%	20%	0%	0%			
RF	Friedman et al, 1988 ⁹	39	54%	13%	0%	33%			
RF	Ishijima et al, 1988 ³⁸	19	82%	18%	0%	0%			
RF	Young, 1990 ³⁶	18	75%	1070	070	25%			
RF	Kumagai et al, 1992 ⁵⁰	7	29%	14%	57%	0%			
RF	Thomas and Kitchen, 1994 ¹²	44	68%	1170	11%	21%			
RF	Fazl et al, 1995 ⁶²	4	0070	100%	0%	2170			
RF	Rath et al, 1997 ⁵⁸	23	57%	10070	26%	17%			
RF	Samii et al, 2001 ¹⁰	47	63%		37%	0%			
RF	Tomáš and Haninec, 2005 ⁵⁷	21	62%		38%	0%			
RF	Ali et al, 2011 ¹⁴	11	55% (P)		18% (P)	27% (P)			
ni -	All et al, 2011		27% (C)		0% (C)	73% (C)			
RF	Awad et al, 2013 ³⁴	10	60% (30% "complete	")	40% (30% no relie				
RF	Haninec et al, 2014 ⁵⁹	52	71%	, 21%	-070 (50 %) no rene	8%			
Laser	Powers et al, 1984 ⁶⁵	2	100%	21%		0%			
Laser	Powers et al, 1988 ⁶⁴	6	100%	0%		0%			
	Young, 1990 ³⁶	4	50%	0%	50%	0%			
Laser US	Dreval, 1993 ⁶⁸								
	Ko et al, 2016 ⁶¹	124	87%	0 220/	13%	220/			
Various	NO et al, 2016	15	33% (13% "complete") 33%		33%			

C, continuous pain component; MDT, microsurgical DREZotomy; P, paroxysmal pain component; RF, radiofrequency; US, ultrasound. ^aModified procedure not incorporating microknife incision. ^bModified procedure also incorporating microblade lesioning of cord.



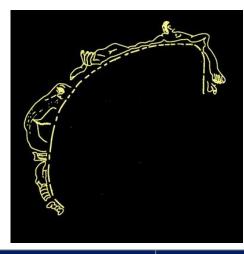
- Paroxysmal painful discharges: ablative procedures
- DREZotomy: 50–75% of the paroxysmal pain

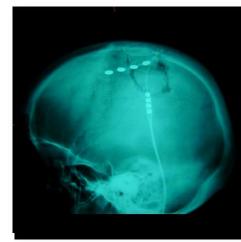
less in inconstant pain/10% of patients

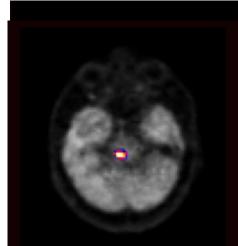
- · Complications: ipsilateral lower limb weakness and ataxia,
- 13–20% recurrence (constant pain)
- Final FU acceptable pain control in 60%



Motor cortex stimulation







Ahthors/years	Type of pain	N	Improvement (%)	Follo wup (m)
Tsubokawa et al. 1991	Central pain	12	75	2
Nguyen et al. 2000	Neuropathic pain	13	77	
Teixeira et al. 1996	Neuropathic pain	9	66	18
Meyerson 1993	Periphersl neuropathic pain	6	50	
Katayama et al. 2001	Neuropathic pain	9	48	
Rainov et al. 1997	Facial pain	2	100	18
Nguyen et al. 1999	Facial pain	12	83	27
Teixeira et al. 1998	Facial pain	3	67	32
Nguyen et al. 2000	Myelopathic pain	3	33	
Katayama et al. 1994	Wallerberg'syndrome	3	66	6
Teixeira et al. 2006	BPA	8	83	8
Katayama et al. 2001	Phantom limb pain	5	20	
Teixeira et al. 2006	Complex regional pain syndrome	2	100	14





Operculo-insular cortex TMS stimulation

Targeting the insula

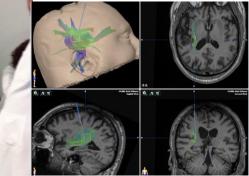
Postero-superior insula TMS

- Did not affect thermal detection thresholds or heat pain thresholds/baseline values
- Cold pain threshold decreased (towards analgesia) 1 hour after the stimulation ns

Table 1 Thermal thresholds measured by quantitative sensory testing and distances from the scalp to targets.

Distances and thresholds	N	Minimum	Maximum	Mean	Std. Deviation	Related samples Wilcoxon's Signed Rank Test (P)
RMT_TA (%MSO)	7	39	83	54.43	16.092	
Distance between skull and insula (mm)	7	43.0	53.7	48.814	4.1755	
Distance between skull and LL M1 (mm)	7	38.3	51.8	47.114	4.8057	0.240
CDT_LUP_B (°C)	7	22.4	30.8	29.214	3.0394	0.00/
CDT_LUP_A (°C)	7	26.0	30.7	28.871	1.8200	0.396
WDT_LUP_B (°C)	7	32.9	39.3	34.871	2.1523	0.000
WDT_LUP_A (°C)	7	33.1	36.4	33.900	1.1460	0.093
HPT_LUP_B (°C)	7	39.5	46.8	43.529	2.8582	0.20/
HPT_LUP_A (°C)	7	39.8	48.2	44.029	3.1495	0.396
CPT_LUP_B (°C)	7	9.7	25.2	17.957	5.4052	0.0/4
CPT_LUP_A (°C)	7	3.8	20.3	12.543	6.1321	0.061

CDT: cold detection threshold; WDT: warm detection threshold; HPT: heat pain threshold; CPT: cold pain threshold; LUP: left upper limb; LL: lower limb; M1: primary motor cortex; B: baseline; A: after; RMT: rest motor threshold; TA: tibialis anterior muscle; MSO: maximal stimulator output.



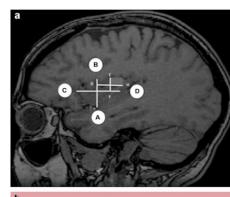


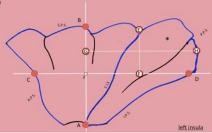




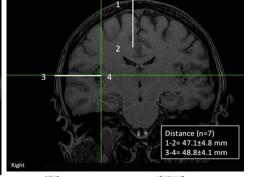
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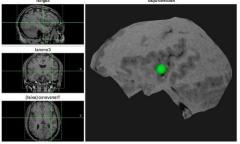
Into the Island: A new technique of non-invasive cortical stimulation of the insula

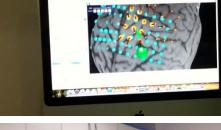




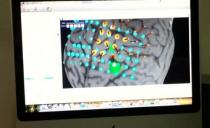












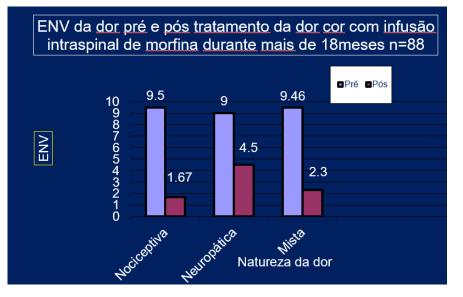




Intrathecal infusion of drugs

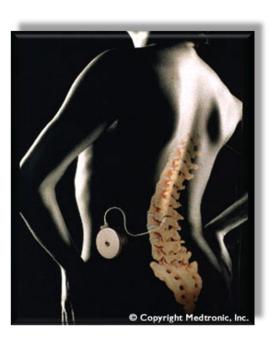
Drugs: opioids, Ca++ channel antagonists, NMDA antagonists, GABA agonists, alpha-2-adrenergic

agonists, acetylcholinesterase inhibitors and somatostatin analogue





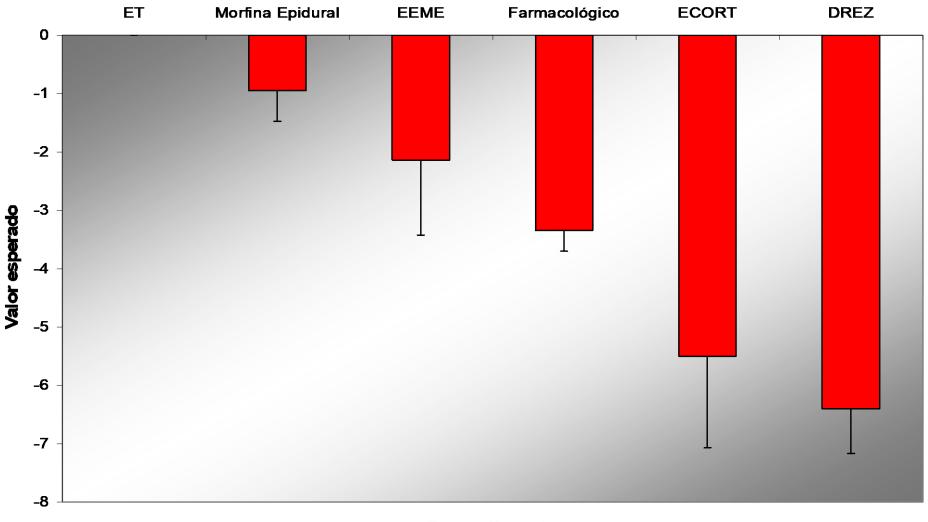








Expected values and standard errors of variations in the VAS pain score for each procedure





Procedimento

Conclusions

- Neuropathic pain is very frequent in patients with brachial plexus injury,
- Several mechanisms: peripheral nociceptor sensitization, peripheral ectopic discharges, central sensitization in the dorsal horn, and cortical reorganization, sensitization and neuroplasticity.
- Pain severity similar in patients with mixed pain and neuropathic pain
- The impact on pain sensatiions, mood, quality of life and physical disability higher on the mixed pain patients
- The impact in the physical components higher than in the psychic and mental dimensions in mixed pain patients
- The disability is greater for bi-manual skills, strength, and sleep in mixed pain patients
- There are differences in the cortical plasticity between neuropathic and mixed pain patients
- Treatment: pharmacological measures, non-pharmacological strategies, topical agents, physiotherapy, and rehabilitation programs
- Surgical options: nerve repair or nerve transfer, DREZ, spinal cord stimulation for non-avulsion neuropathic pain,

cortical and posterior insula stimulation for constant pain

