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Withdrawal response in healthy adults

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Abstract

Background: Withdrawal response was used to explain extensor plantar response in population without pyramidal dysfunction but there is lack of data characterizing this response in normal population. *Objective:* To characterize withdrawal response from pain and tickle sensation in population without any neurological deficit. *Methods:* The study was carried out using four different stimuli, namely heat-induced pain, cold-induced pain, electric-induced pain using electromyography stimulator and ticklish sensation using superworm (*Zophobas morio),* applied to normal subjects in University Malaya Medical Centre, Kuala Lumpur. *Results:* Heat-induced pain resulted in flexion of the big toe (61.1%), other toes (62.3%), ankle dorsiflexion (82.6%), knee flexion (83.9%) and hip flexion (83.9%). Electric-induced pain showed flexion of the big toe (27.7%), other toes (28.3%), ankle dorsiflexion (51.0%), knee flexion (76.0%) and hip flexion (76.0%). Ticklish sensation showed flexion of the big toe (14.8%), other toes (14.8%), ankle dorsiflexion (22.7%), knee flexion (21.9%), and hip flexion (21.9%). There was significant correlation between fear and ticklish sensation induced withdrawal responses and extension of big toe. Cold induced pain resulting in big toe flexion (6.4%), other toes (6.9%), dorsiflexion of ankle (7.1%), flexion of knee (6.9%), and hip flexion (6.9%). Females were more responsive to heat, males to electrical stimulation. The prevalence of big toe extension ranged from 11.0% (electrical), 6.3% (ticklish), 4.8 (heat), to 0% (cold), a mean of 5.2% overall.
Conclusion: Withdrawal response caused by nociceptive and ticklish sensation consists mostly of big toe flexion and of other toes, ankle dorsiflexion and flexion of the knee and hip. Extension of the big toe is seen in about 5% of all the stimulation.

INTRODUCTION

The plantar reflex (also known as plantar response) is a nociceptive segmental spinal reflex that functions, to protect the sole of the foot.[1] However, interpretation of the plantar reflex remains an art. When flexion of the big toe is observed (which is usually accompanied by flexion and adduction of other toes), it is termed flexor plantar reflex, which is interpreted as a normal response. If extension of big toe is observed (which is usually accompanied by extension and abduction of other toes), this is termed extensor plantar reflex or Babinski's sign.[1-3] Babinski's sign is well accepted as a sign of upper motor neuron lesion. Babinski's sign may also be obtained in states of unconsciousness, profound sleep, deep anaesthesia or drug intoxication, and after electroconvulsive therapy.[4]

There are several Babinski's mimickers, which can present with extension of big toe. (1) Pseudo Babinski's sign can be seen in patients with choreoathetosis, in which the extension of big toe is due to hyperkinesia.[5] (2) In patients with inversion of plantar reflex, in which the short flexors of toe are paralyzed or the tendons severed, extension of great toe is obtainable.[5] (3) Extension of the big toe can be a withdrawal response, and is hypothesized to be caused by ticklish and nociceptive sensation.[4]

Patients who are found to have extension of the great toe on plantar stimulus, with no apparent pyramidal dysfunction, are commonly interpreted to have a withdrawal response by the clinician. In fact, withdrawal response is often referred to as the flexor withdrawal reflex, flexor reflex or nociceptive reflex, which consists of flexion of the ankle, knee, and hip when the foot is painfully stimulated. Dejong referred to it as voluntary withdrawal response.[4] Though there is variability in the definition of the withdrawal response, it is mainly used to explain extensor plantar responses in populations without pyramidal dysfunction. This response is believed to be a voluntary movement, caused by nociceptive or ticklish sensations[4], and often confused with Babinski's sign. The examiner is required to repeat the stimulus more gently while holding the foot

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and ankle in order to eliminate the voluntary withdrawal. In contrary, a true Babinski's sign is claimed to be reproducible.[5]

Despite its importance in daily clinical practice, there is no previous study characterizing this response in normal populations. Hence, we performed this study to characterize the withdrawal response from pain and ticklish sensation in healthy adults. We were particularly interested to investigate how these responses can mimic a Babinski's sign.

METHODS

Heat, cold and electric stimuli were used as nociceptive stimuli. Our preliminary study revealed the medial side of the mid-plantar surface as the most sensitive area with highest number of positive responses as compared with other areas on the foot. Hence, the mid-medial sole was selected as region for heat and cold stimulation. For electrically induced pain, ring electrodes were wound around the big toe. Ticklish sensation was tested using superworm (larvae stage of *Zophobas morio*).

Medical students from University of Malaya, age ranges from 18 to 25 years old, without previous or on-going neurological problem, were recruited and randomly allocated to various study modalities. All subjects were required to lie in the supine position with full extension of all their limbs, asked to relax and open their eyes to avoid hypervigilance. Withdrawal response was produced using 4 different modalities, i.e. heat induced pain, cold induced pain, electric induced pain and ticklish sensation.

Pain can be experimentally produced with heat above 45°C, cold below 15°C and electrical stimuli.[6-8] Tickle, a light or feather-type noxious sensation termed by Hall and Allin as knismesis, can be triggered by light touch, light electrical current and crawling insects.[9,10] In this study, heat induced pain was produced using a tuning folk immersed in boiling water for 5 minutes. The base of the tuning folk was put on the medial side of mid-plantar surface for a maximum of 0.5 second. A metronome was used to limit the duration of contact. Cold induced pain was produced using ice cube placed on the medial side of mid-plantar surface for a maximum of 2 seconds. Electric induced pain was produced using ring electrode connected to an electromyography stimulator and tied around the big toe. An electrical stimulation of 100 milliampere lasting for 1 millisecond was applied. Ticklish sensation was produced using a superworm (larvae stage of *Zophobas morio*) placed on the feet of the subject. Subjects were required to inform if they were fearful of the worm.

Each step was performed on both sides of the feet and repeated thrice with video recording. The response was documented as (a) flexion, extension or no movement of big toe, (b) flexion, extension or no movement of other toes, (c) dorsiflexion, plantar-flexion or no movement of the ankle, (d) flexion, extension or no movement of the knee, and (e) flexion, extension or no movement of the hip. Triple flexor response was defined as the combination of ankle dorsiflexion, knee and hip flexion.

Analysis was performed using statistical package SPSS version 16.0 and significant level was set at a p-value less than 0.05.

RESULTS

Fifty-three subjects, with 43.4% males, were recruited for stimulation with heat-induced pain. Each subject was tested thrice on each foot, except one subject who refused a third attempt, making a total of 316 attempts. The most prevalent movements were flexion of big toe (61.1%), flexion of other toes (62.3%), ankle dorsiflexion (82.6%), knee flexion (83.9%) and hip flexion (83.9%), as shown in Table 1. Extension of the big toe was seen in 4.8% of the attempts. Females had higher frequency of extension of the big toe, flexion of the big toe and triple flexor response (p-value < 0.05). There were 5 subjects (9.43%) who had extension of the big toe, of which, 2 (40.0%) had persistent extension of big toe in all three attempts.

Sixty-three subjects, with 57.1% males, were recruited for stimulation with cold-induced pain. Each subject was tested for 3 attempts on each foot, making a total of 378 attempts. Table 2 showed that most of the subjects had no response in all joints. Among the positive responses, the most prevalent movements were flexion of big toe (6.4%), flexion of other toes (6.9%), ankle dorsiflexion (7.1%), knee flexion (6.9%) and hip flexion (6.9%). None of the attempts produced extension of big toe. There was no significant difference between male and female for triple flexor response.

Fifty subjects, half was male, were recruited for stimulation with electric-induced pain. Each subject was tested for 3 attempts on each foot, making a total of 300 attempts. Referring to Table 3, most subjects showed no movement in big toe

Table 1: Frequency and percentage of the responses of big toe, other toes, ankle, knee and hip to heat induced pain, in total and according to sex

		Male		Female		Total	
		f	%	*f*	%	*f*	%
Big toe	Extension	1	0.3	14	4.4	15	4.8
	Flexion	82	26.0	111	35.1	193	61.1
	No movement	55	17.4	53	16.8	108	34.2
	Total	138	43.7	178	56.3	316	100.0
Other toes	Extension	1	0.3	14	4.4	15	4.8
	Flexion	86	27.2	111	35.1	197	62.3
	No movement	51	16.1	53	16.8	104	32.9
	Total	138	43.6	178	56.3	316	100.0
Ankle	Dorsiflexion	103	32.6	158	50.0	261	82.6
	Plantar-flexion	0	0.0	1	0.3	1	0.3
	No movement	35	11.1	19	6.0	54	17.1
	Total	138	43.7	178	56.3	316	100.0
Knee	Extension	0	0.0	0	0.00	0	0.00
	Flexion	100	31.7	165	52.2	265	83.9
	No movement	38	12.0	13	4.1	51	16.1
	Total	138	43.7	178	56.3	316	100.0
Hip	Extension	0	0.0	0	0.00	0	0.00
	Flexion	100	31.7	165	52.2	265	83.9
	No movement	38	12.0	13	4.1	51	16.1
	Total	138	43.7	178	56.3	316	100.0

f, frequency of movements

Table 2: Frequency and percentage of the responses of big toe, other toes, ankle, knee and hip to cold induced pain, in total and according to sex

		Male		Female		Total	
		f	%	*f*	%	*f*	%
Big toe	Extension	0	0.0	0	0.0	0	0.00
	Flexion	21	5.6	3	0.8	24	6.4
	No movement	195	51.6	159	42.1	354	93.6
	Total	216	57.2	162	42.9	378	100.0
Other toes	Extension	0	0.0	0	0.00	0	0.00
	Flexion	23	6.1	3	0.8	26	6.9
	No movement	193	51.1	159	42.1	352	93.1
	Total	216	57.2	162	42.9	378	100.0
Ankle	Dorsiflexion	14	3.7	13	3.4	27	7.1
	Plantar-flexion	0	0.0	0	0.0	0	0.0
	No movement	202	53.4	149	39.4	351	92.9
	Total	216	57.1	162	42.8	378	100.0
Knee	Extension	0	0.0	0	0.00	0	0.00
	Flexion	16	4.2	10	2.7	26	6.9
	No movement	200	52.9	152	40.2	352	93.1
	Total	216	57.1	162	42.9	378	100.00
Hip	Extension	0	0.00	0	0.00	0	0.0
	Flexion	16	4.2	10	2.7	26	6.9
	No movement	200	52.9	152	40.2	352	93.1
	Total	216	57.1	162	42.9	378	100.0

f, frequency of movements

Table 3: Frequency and percentage of the responses of big toe, other toes, ankle, knee and hip to electric induced pain, in total and according to sex

		Male		Female		Total	
		f	%	*f*	%	*f*	%
Big toe	Extension	24	8.0	9	3.0	33	11.0
	Flexion	42	14.0	41	13.7	83	27.7
	No movement	84	28.0	100	33.3	184	61.3
	Total	150	50.0	150	50.0	300	100.0
Other toes	Extension	26	8.7	16	5.3	42	14.0
	Flexion	42	14.0	43	14.3	85	28.3
	No movement	82	27.3	91	30.3	173	57.7
	Total	150	50.0	150	50.0	300	100.0
Ankle	Dorsiflexion	91	30.3	62	20.7	153	51.0
	Plantar-flexion	0	0.00	6	2.0	6	2.0
	No movement	59	19.7	82	27.3	141	47.0
	Total	150	50.0	150	50.0	300	100.0
Knee	Extension	0	0.0	0	0.0	0	0.0
	Flexion	131	43.7	97	32.3	228	76.0
	No movement	19	6.3	53	17.7	72	24.0
	Total	150	50.0	150	50.0	300	100.0
Hip	Extension	0	0.0	0	0.00	0	0.0
	Flexion	131	43.7	97	32.3	228	76.0
	No movement	19	6.3	53	17.7	72	24.0
	Total	150	50.0	150	50.0	300	100.0

f, frequency of movements

Table 4: Frequency and percentage of the responses of big toe, other toes, ankle, knee and hip to ticklish sensation, in total and according to sex

		Male		Female		Total	
		f	%	*f*	%	*f*	%
Big toe	Extension	5	1.4	18	4.9	23	6.3
	Flexion	42	11.5	12	3.3	54	14.8
	No movement	163	44.5	126	34.4	289	78.9
	Total	210	57.4	156	42.6	366	100.0
Other toes	Extension	5	1.4	18	4.9	23	6.3
	Flexion	42	11.5	12	3.3	54	14.8
	No movement	163	44.5	126	34.4	289	78.9
	Total	210	57.4	156	42.6	366	100.0
Ankle	Dorsiflexion	41	11.2	42	11.5	83	22.7
	Plantar-flexion	5	1.4	1	0.3	6	1.6
	No movement	164	44.8	113	30.9	277	75.7
	Total	210	57.4	156	42.7	366	100.0
Knee	Extension	0	0.0	0	0.0	0	0.0
	Flexion	43	11.8	37	10.1	80	21.9
	No movement	167	45.6	119	32.5	286	78.1
	Total	210	57.4	156	42.6	366	100.0
Hip	Extension	0	0.0	0	0.0	0	0.0
	Flexion	43	11.8	37	10.1	80	21.9
	No movement	167	45.6	119	32.5	286	78.1
	Total	210	57.4	156	42.6	366	100.0

f, frequency of movements

and other toes. The most prevalent movements of big toe and other toes were flexion, 27.7% and 28.3% respectively. Prevalence of extension of big toe and other toes were 11.0% and 14.0%. Other prevalent movements were ankle dorsiflexion (51.0%), knee extension (76.0%) and hip flexion (76.0%) respectively. Male had higher tendency to yield extensor big toe and triple flexor response with electric induced pain (p-value< 0.05). There were 9 subjects with extension of big toe in at least one of the 3 attempts, of which, 6 subjects (66.7%) showed persistent extension of big toe in all attempts.

Sixty-one subjects, with 35 males, were recruited for stimulation with ticklish sensation. Each subject was tested for 3 attempts on each foot, making a total of 366 attempts. From Table 4, most subjects had no movements in all the joints. The commonest positive movements were flexion of big toe (14.8%), flexion of other toes (14.8%), ankle dorsiflexion (22.7%), knee flexion (21.9%) and hip flexion (21.9%). There was no significant difference in triple flexor response and extension of big toe between male and female. There were 5 subjects with extension of big toe, in which 3 (60.0%) had persistent extension of big toe in all attempts. Subjects fearful to superworm had 9 times higher tendency to yield any movement over the joints compared to non-fearful group (Table 5). Up-going big toe was only elicited in those who were fearful of the worm.

In general, heat and electrical induced pain were more likely to provoke withdrawal responses followed by ticklish sensation and cold stimulation. In total, as shown in Table 6, knee and hip flexion (44%) is the most prevalent withdrawal response, followed by dorsiflexion of the ankle (38.5%), flexion of big toe (26.6%) and extension of big toe (5.2%).

The prevalence of big toe extension ranges from 11.0% (electrical), 6.3% (ticklish), 4.8 (heat), to 0% (cold), with a mean of 5.2% overall. In total, 114 out of 1,360 attempts yielded extension of big toe. Sub-analysis on this group showed that extension of big toe was commonly associated with extension of other toes, ankle dorsiflexion and knee-hip flexion (64.9%, 78.9% and 92.1% respectively).

DISCUSSION

This study on withdrawal response in healthy adults shows that the most prevalent withdrawal response consists of toes flexion, ankle dorsiflexion and knee-hip flexion. Heat and electrical induced pain provoke more withdrawal responses followed by ticklish sensation and cold stimulation.

This study also shows that big toe extension is not a common feature in withdrawal response, with a mean prevalence of only 5.2%. Sub-analysis shows that big toe extension is commonly associated with extension of other toes (64.9%), as well as triple flexor response. This could

Table 5: Correlation between fear to superworm and withdrawal responses

		Emotional factor		Odd ratio (95% CI)	p-value (using chi-square)
		Fearful	Not fearful		
Big toe movement (both extension and flexion)	Presence	71 (30.3%)	6 (4.5%)	9.1	<0.05
	Absence	163	126		
	Total	234	132		
Extension of big toe	Presence	23 (9.8%)	0 (0%)	∞	Not applicable
	Absence	211	132		
	Total	234	132		
Other toes movement	Presence	71 (30.3%)	6 (4.5%)	9.1	<0.05
	Absence	163	126		
	Total	234	132		
Ankle movement	Presence	82 (35.0%)	7 (5.3%)	9.6	<0.05
	Absence	152	125		
	Total	234	132		
Hip/knee movement	Presence	74 (31.6%)	6 (4.5%)	9.7	<0.05
	Absence	160	126		
	Total	234	132		

Table 6: Frequency and percentage of withdrawal responses in total of all modalities

		Total (combining all modalities)	
		f	**%**
Big toe	Extension	71	5.2
	Flexion	354	26.0
	No movement	935	68.8
	Total	1360	100
Other toes	Extension	80	5.9
	Flexion	362	26.6
	No movement	918	67.5
	Total	1360	100
Ankle	Dorsiflexion	524	38.5
	Plantar-flexion	13	1.0
	No movement	823	60.5
	Total	1360	100
Knee-hip	Extension	0	0
	Flexion	599	44
	No movement	761	56
	Total	1360	100

f, frequency of movements

possibly be a useful differentiating feature between withdrawal response and true Babinski's sign. Among those with big toe extension, almost half (40.0%, 60.0% and 66.7% with heat, ticklish and electric stimulation respectively) had persistent big toe extension in all three attempts. Therefore reproducible big toe extension can also be a feature in withdrawal response, similar to Babinski's sign.[5]

The majority of the subjects had no withdrawal response in this study. This may be due to inadequate stimulation, or because withdrawal response might be suppressible. Withdrawal response is postulated to be a protective response towards unexpected threat.[1] The participants in this study were informed about the procedure and thus the unexpectedness of the stimulation is reduced. This may allow cortical modulation of the spinal response and suppression of the response in some participants.

We have demonstrated that fear is significantly correlated to withdrawal response, suggesting that fear play an important role in the generation of withdrawal response. Fear increases vigilance to threat[11], thereby may reduce the cortical suppression of the withdrawal response.

The observation that extension of the big toe was only elicited in those with fear has important clinical implication. It should be a subject of further study, as it supports the importance of making patients comfortable and relaxed during neurological examination.

In conclusion, withdrawal responses induced by nociception and ticklish sensation are mostly characterized by flexion of the big toe and other toes, knee and hip flexion with dorsiflexion of ankle. Extension of big toe is seen in only 5% of all stimulations. Fear increases the tendency to develop a withdrawal response.

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