Prognostic factors for recovery in radicular pain caused by lumbar disc herniation



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Overview

- Background
- Aims of the study
- Materials and Methods
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  - Study population paper III/IV
- Results and Conclusions
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  - Paper III
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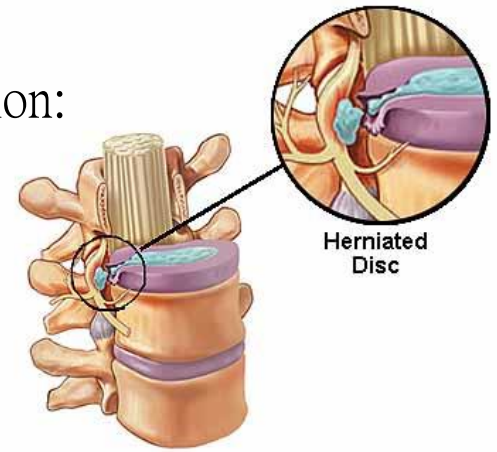
- Clinical implications

Background:

- ✓ Lumbar radicular pain constitutes only 5-10% of low back pain (LBP) conditions, but accounts for 30% of the yearly cost of treatment of LBP*
- ✓ Physical, psychosocial, clinical, surgery-related, radiological and genetic factors influence the recovery from lumbar radicular pain
- ✓ The pathogenesis of radicular pain encompasses mechanical and inflammatory components
- ✓ Inflammatory substances are released following a disk herniation:
  Prostaglandin, bradykinin, NO (nitric oxide)
  Cytokines: Interleukins (IL-1, IL-6, IL-8) and TNF-a



Shvartzman L et al 1992

Aims

The main purpose:

- Investigate prognostic factors for recovery after lumbar radicular pain due to disc herniation (DH)

Aims

Specific aims:

I. Identify predictors for functional outcome, especially to investigate the influence of cytokines (IL-6 and IL-8) at 1-year recovery in patients with lumbar radicular pain

II. Examine how variability of the IL-1 α C>T rs1800587 gene affects the pain intensity and pressure pain threshold (PPT) in patients with symptomatic DH

III. Examine whether Modic changes are associated with pain during 1-year follow-up in patients with lumbar radicular pain

IV. Investigate the interaction between sex and the OPRM1 A118G variant rs1799971, regarding recovery from DH

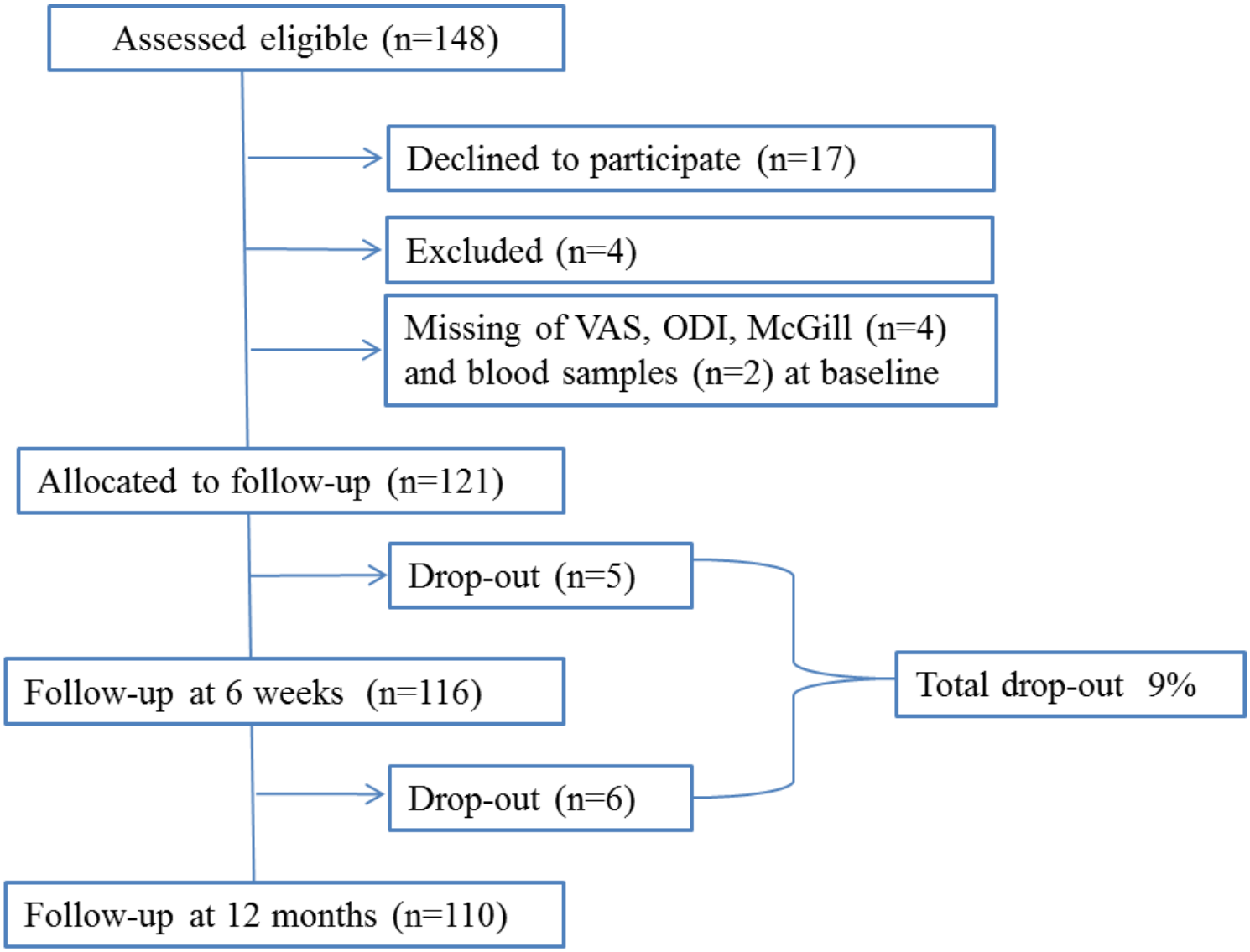
Materials and Methods

- Patients from OUS, Ulleval (papers I - II)
  OUS, Ulleval and HUS (papers III - IV) } 2007 - 2009

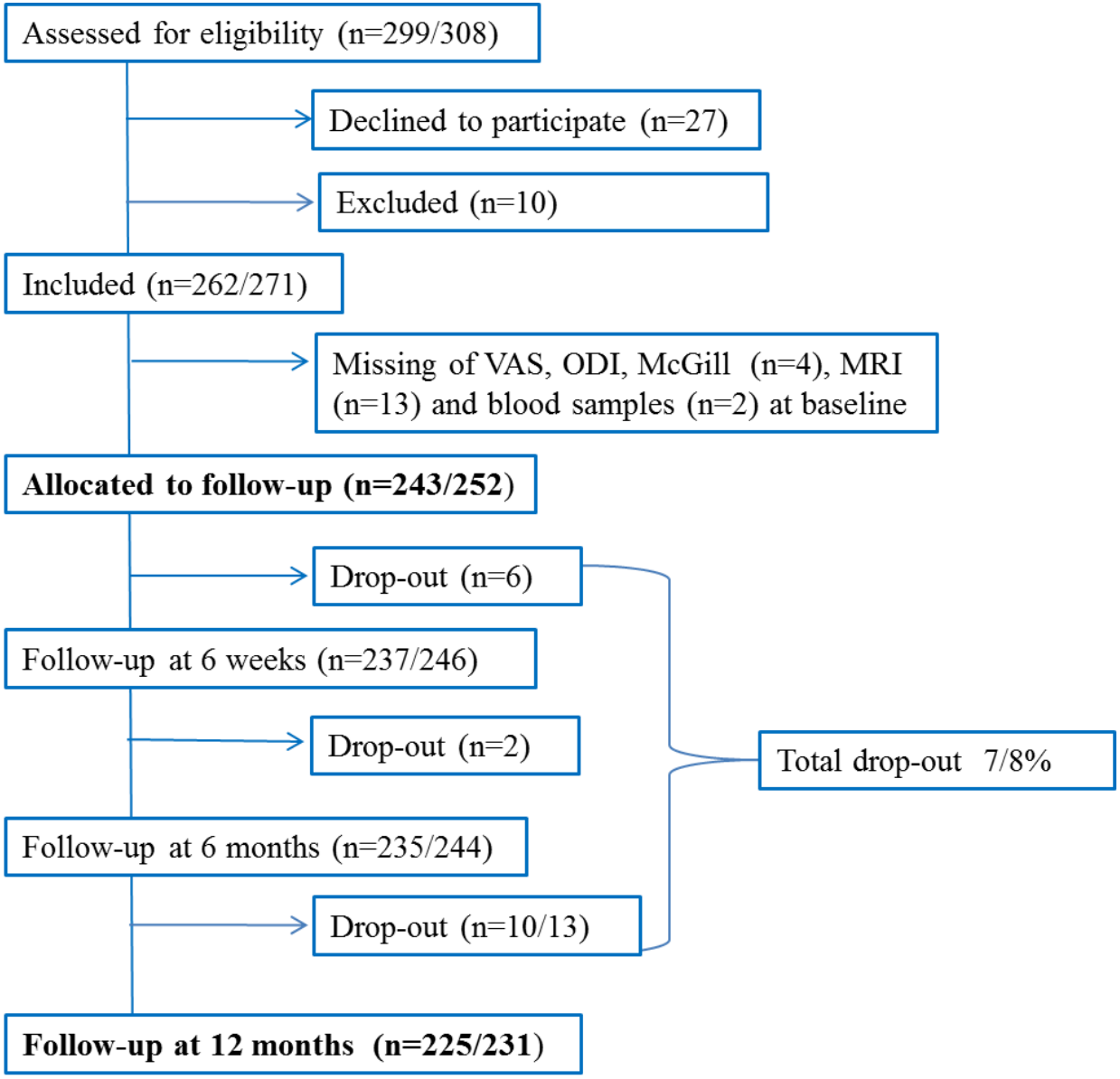
- Inclusion criteria:
  - ✓ Age between 18 and 60 years
  - ✓ Lumbar disc herniation on MRI with corresponding distribution of pain in lower limbs
  - ✓ Positive straight leg raising (SLR) test

- Exclusion criteria: Lumbar spinal stenosis; previous spinal surgery for a herniated disc at the same level or lumbar fusion at any level; generalised musculoskeletal pain; inflammatory rheumatic disease; diabetic polyneuropathy; cardiovascular disease (NYHA III and IV); cancer; psychiatric disease, drug misuse and alcoholism; recent surgery (within 1 month); pregnancy; poor knowledge in the Norwegian language; non-European-Caucasian ethnicity.

Flow paper I/II:



Flow paper III/IV:



Follow-up

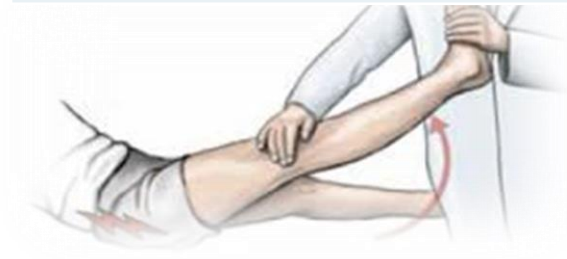
	Pre-treatment (inclusion)	Treatment**	Follow-up		
			6 weeks	6 months	12 months
Paper I (n*=121)	✦				✦
Paper II (n*=121)	✦		✦		✦
Paper III (n*=243)	✦		✦	✦	✦
Paper IV (n*=252)	✦		✦	✦	✦

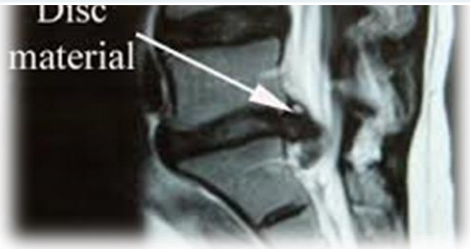
*Allocated to follow-up

**Within 8 weeks from inclusion

Clinical assessment

Clinical examination	
Questionnaires:	VAS (present pain, activity, rest, LBP, leg pain) (0-10)
	Norwegian version of the McGill Pain Questionnaire (MPQ)
	Norwegian version of the Oswestry Disability Index (ODI)
	Registration of sociodemographic variables and work-related factors
Pressure pain threshold (PPT)	
Image evaluation (MRI)	
ELISA measurements of cytokine concentration in serum	
Single nucleotide polymorphism (SNP) genotyping	





Results. Paper I

Independent variables at baseline	Adjusted results			
	β	**B**	**95% CI for B**	***p*-value***
IL-6 protein (pg/ml)	-0.18	-3.41	-5.52 to -1.30	$p = 0.002$
Surgery (yes vs. no)	0.22	7.03	1.21 to 12.84	$p = 0.018$
VAS for back pain (1 cm increase)	-0.33	-2.28	-3.21 to -1.35	$p < 0.001$
High education (no vs. yes)	0.15	5.57	0.66 to 10.47	$p = 0.027$
ODI (per unit)	0.67	0.75	0.58 to 0.93	$p < 0.001$

*Statistics: multiple linear regression analyses with **ODI change** as the dependent variable.

Paper I

Independent variables at baseline	Adjusted results			
	β	B	95% CI for B	*p*-value*
IL-6 protein (pg/ml)	0.29	0.81	0.32 to 1.29	$p = 0.001$
VAS for LBP (1 cm increase)	0.31	0.35	0.15 to 0.55	$p = 0.001$
Duration of radicular pain (weeks)	0.25	0.04	0.01 to 0.07	$p = 0.006$

*Statistics: multiple linear regression analyses with **VAS leg pain** as the dependent variable

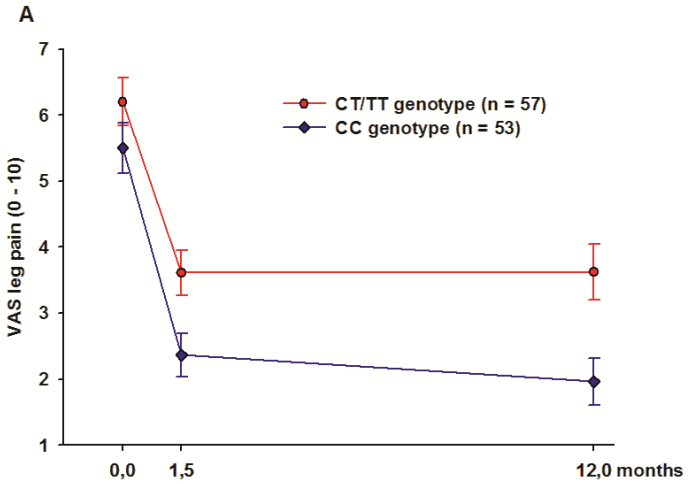
Conclusions

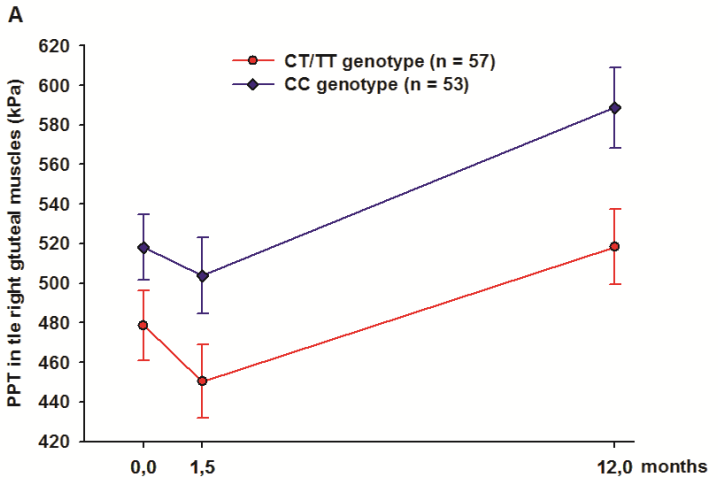
Paper I:

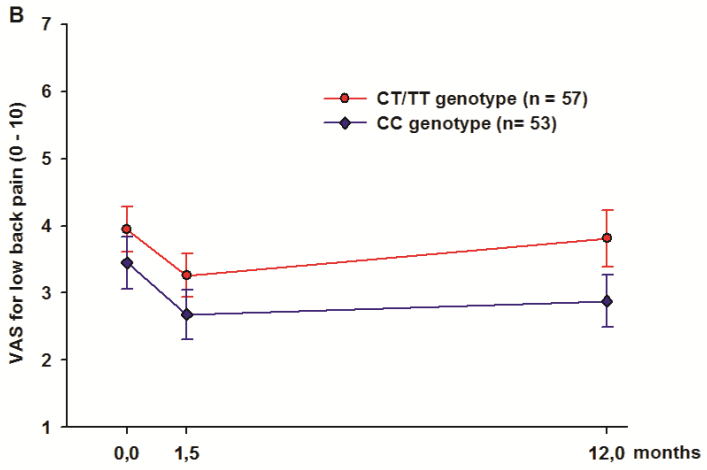
- ✓ High serum IL-6 levels were associated with less favourable recovery in patients with lumbar radicular pain
- ✓ Intense initial back pain, non-surgical treatment, lower educational level, and longer duration of radicular pain before treatment also correlated with a slower recovery the first year after disc herniation

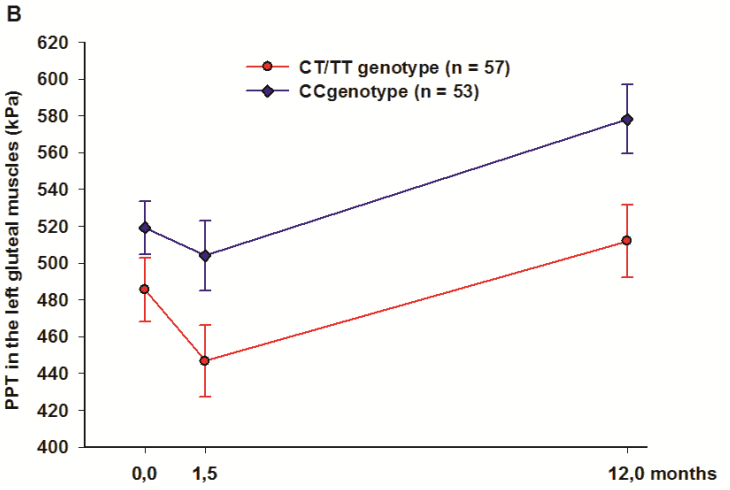
Results. Paper II

IL-1α C>T









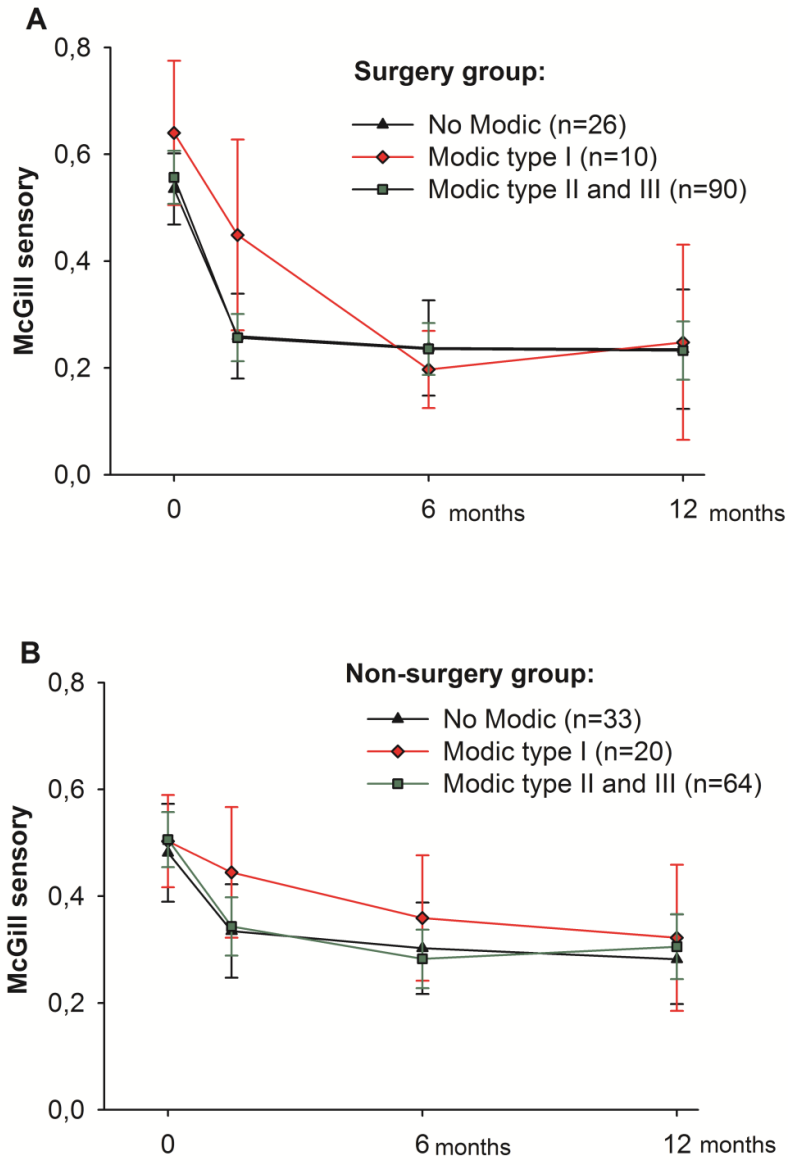
*Statistics: rmANOVA

Conclusion

Paper II:

- ✓ The IL-1α CT/TT genotype rs1800587 may be associated with increased pain intensity, and correspondingly reduced PPT during the first year after disc herniation

Results. Paper III



- ✓ Pain scores had decreased significantly at the 1-year follow-up
- ✓ Modic type was significantly related to McGill sensory scores (mixed model: p=0.014 – 0.026; ANOVA: p=0.007 at 6 weeks), but not to VAS back pain or VAS leg pain scores
- ✓ At 6 weeks, the mean **McGill sensory score was higher in Modic I** than in Modic II – III patients (p=0.003) and in patients without Modic changes (p=0.018)
- ✓ Modic size L1 – S1 was not associated with pain outcomes

Conclusions

Paper III:

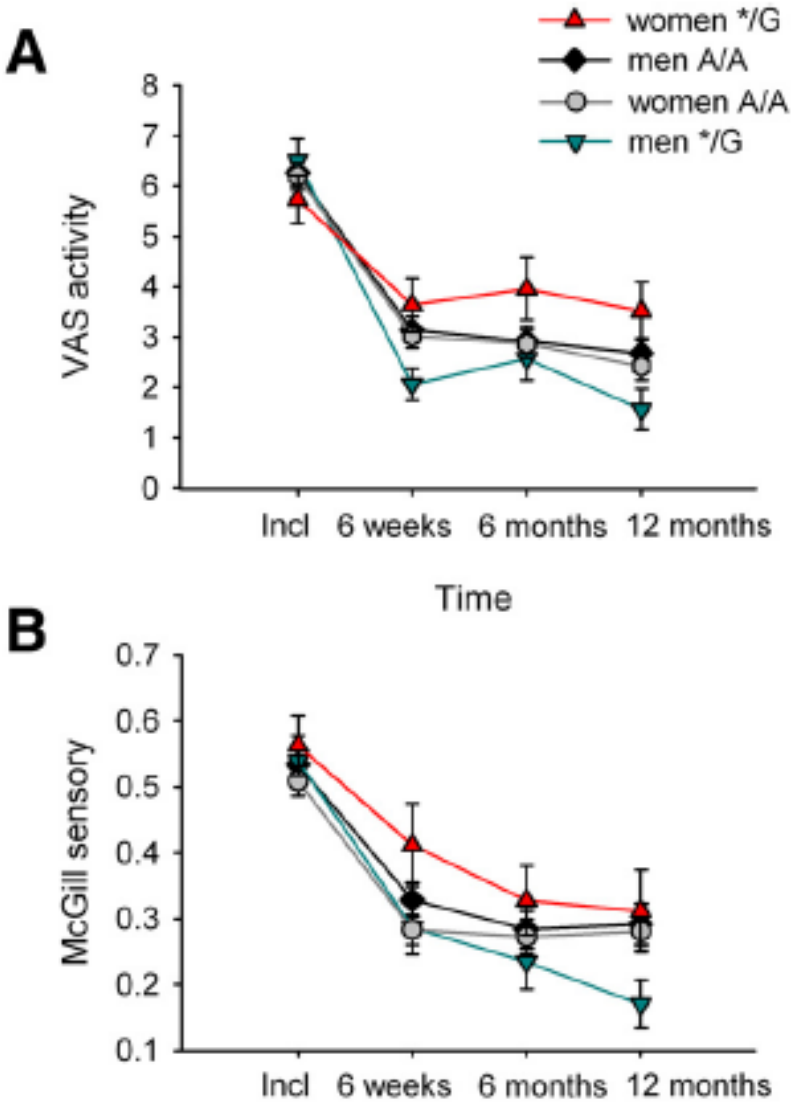
- ✓ Substantial reduction in back and leg pain during the first year

- ✓ Patients with Modic type I changes may, however, have a slower decrease in the McGill sensory pain score than other patients

- ✓ The size of Modic changes does not seem to be associated with McGill sensory pain, VAS back pain, or VAS leg pain scores

Results. Paper IV

OPRM1 A>G



- ✓ The data revealed a significant interaction between sex and A118G genotype regarding the pain intensity during the 12 months (VAS, p=0.002; McGill, p=0.021; rmANOVA)
- ✓ The */G women had 2.3 times as much pain as the */G men 12 months after the disc herniation (VAS, p=0.043, one-way ANOVA; p=0.035, Tukey HSD)
- ✓ In contrast, the A/A women and A/A men seemed to have almost exactly the same recovery rate

Conclusions

Paper IV:

- ✓ The OPRM1 118G allele was associated with increased pain intensity in women, but reduced pain intensity in men the first year after a disc herniation

- ✓ This finding strongly supports the hypothesis that the OPRM1 118G allele may influence the endogenous pain modulatory system differently depending on sex

Clinical implications

- Further studies on the use of serum IL-6 levels as a biomarker in clinical practice are needed, especially with regard to targeted treatment
- The association between IL-1α CT/TT genotype and increased pain intensity or decreased pressure pain threshold may be relevant for future research regarding choice of treatment
- The increased sensory pain in patients with Modic type I may be significant in conveying information to these patients about the expected recovery, and that longer follow-up may be desirable
- The interaction between OPRM1 G allele and sex suggests that gender differences in recovery rate may have a biological genetic explanation

Thank you for your attention

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