Sex differences in the expression of cardiac remodeling and inflammatory cytokines in patients with obstructive sleep apnea and atrial fibrillation

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COI Disclosure

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Disclosure

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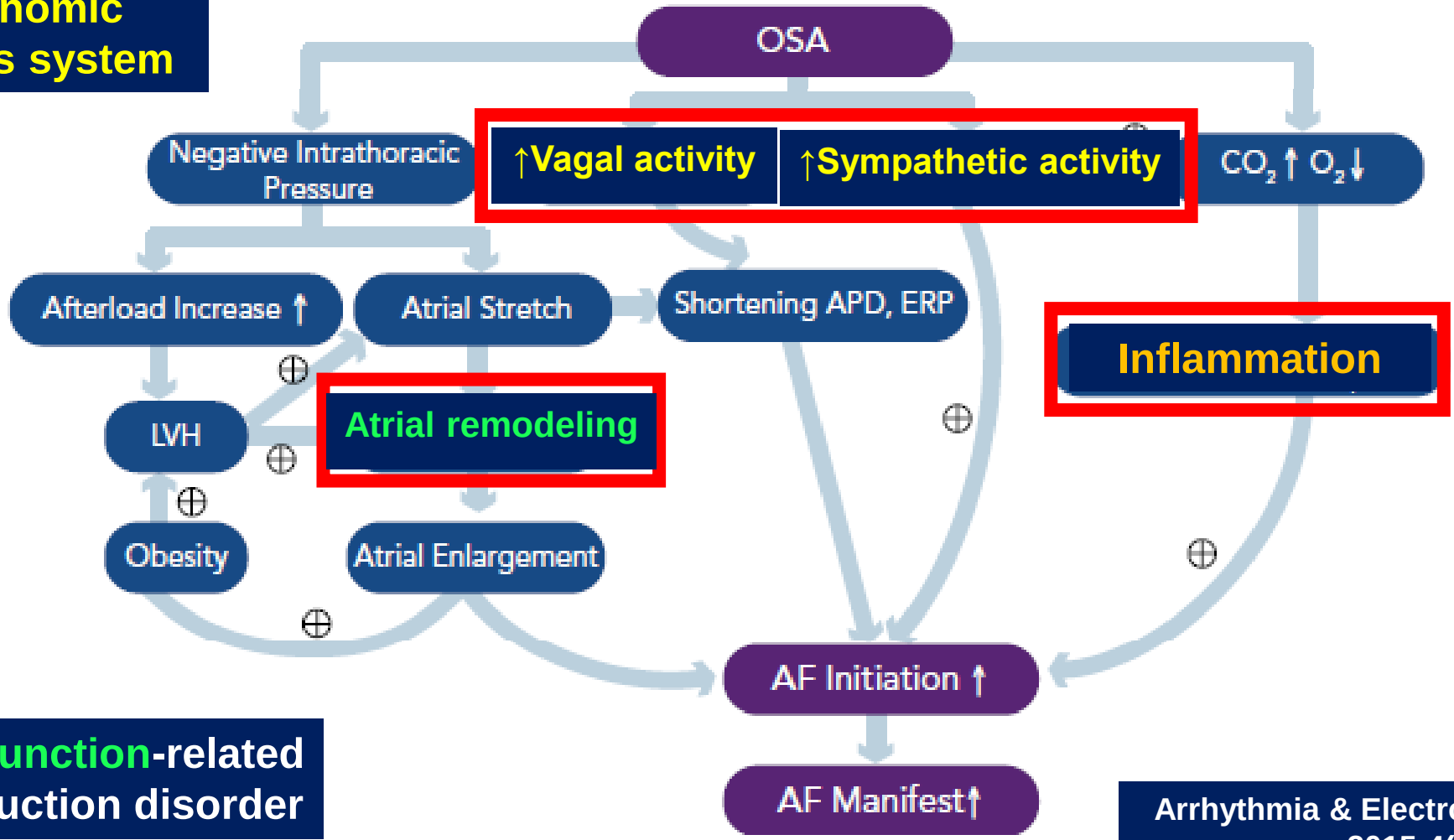
Mechanism of AF development in OSA patients

Autonomic nervous system



Gap junction-related conduction disorder

Arrhythmia & Electrophysiology Review 2015;4(1):14-8

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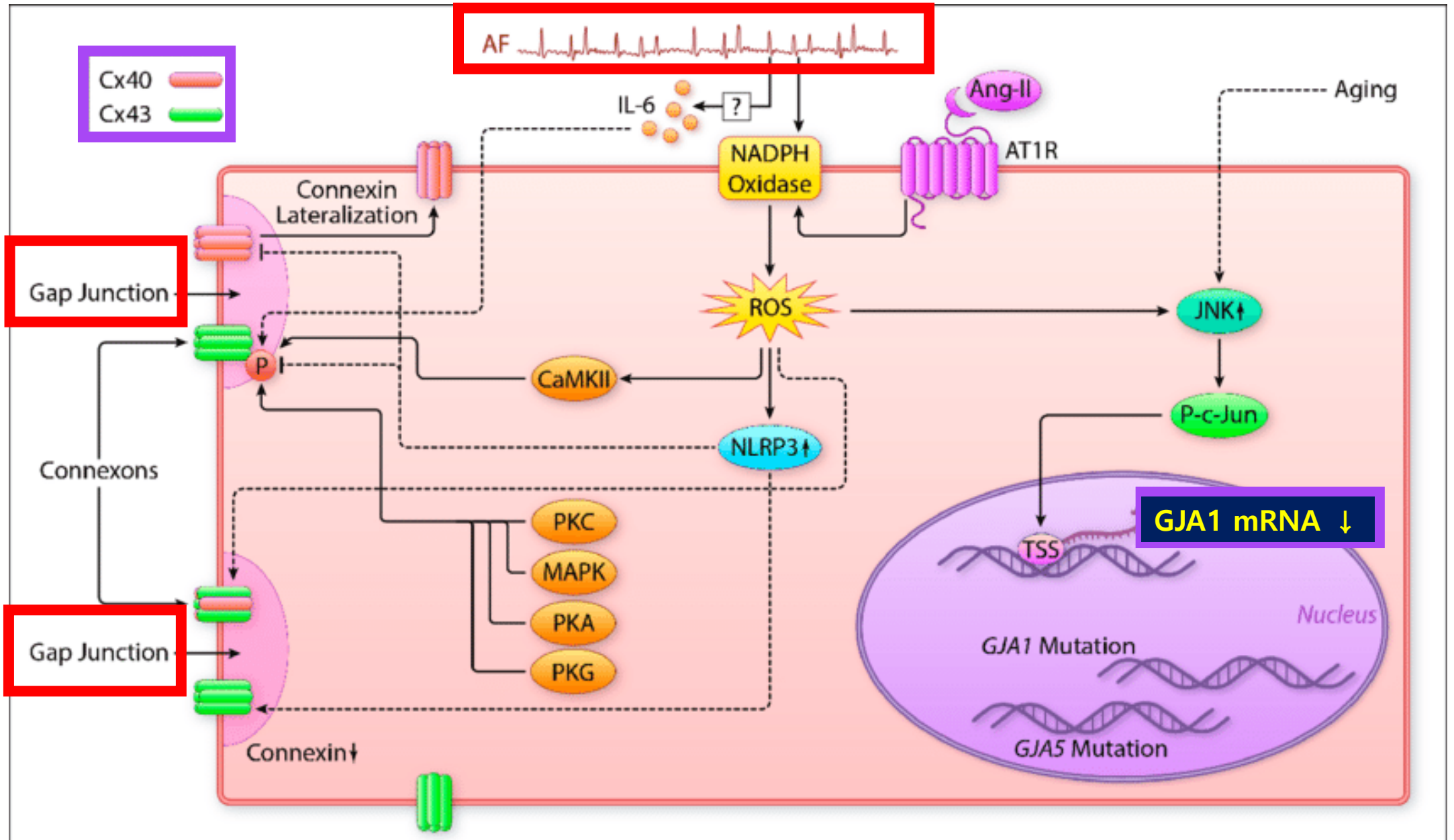

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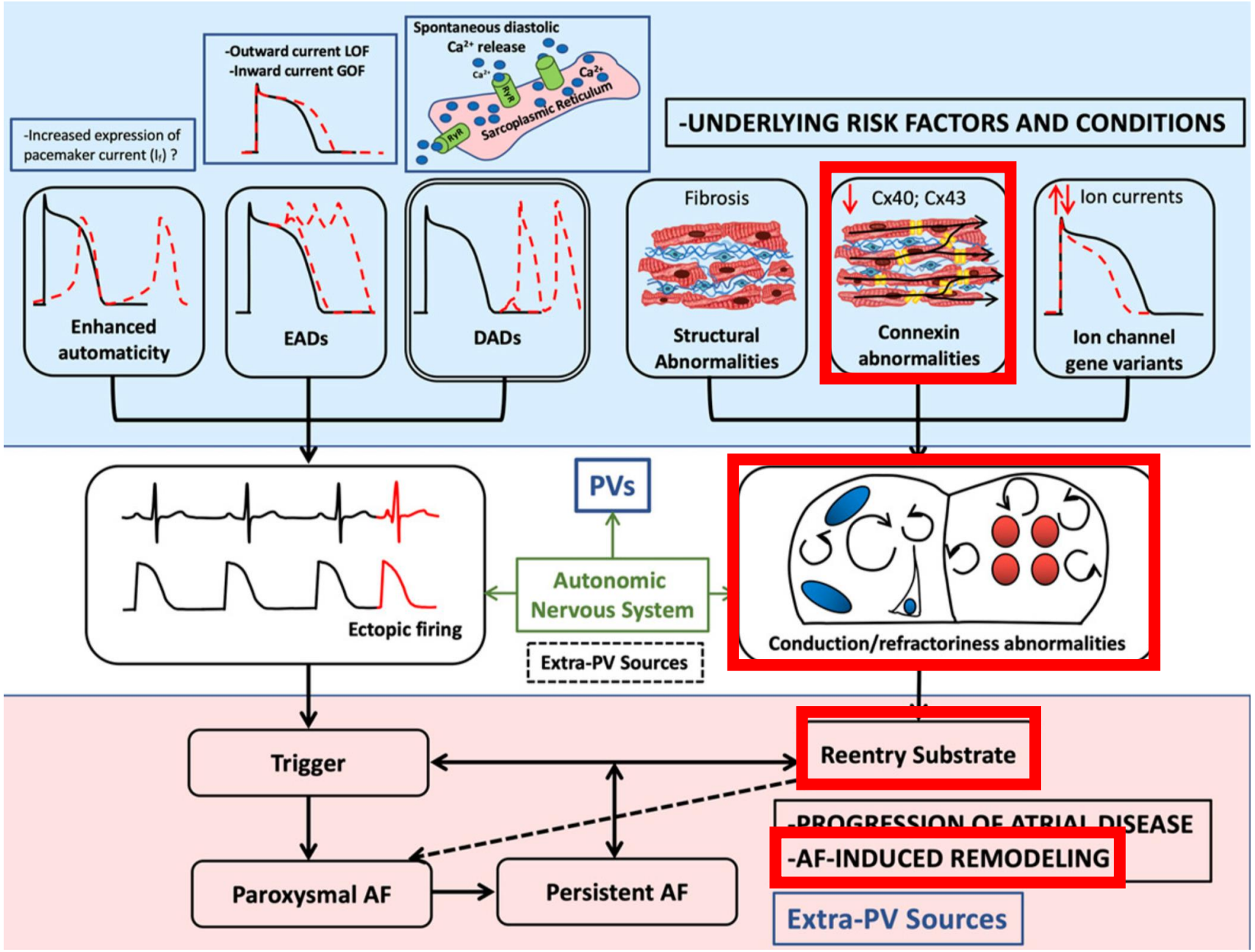

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Aim

- **OSA & AF:**
  - ✓ **Different sexes, different mechanisms ?**
    - **Risk factors**
    - **Cardiac remodeling**
    - **Biomarkers**

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Methods & Statistics

- Sleep-related breathing disorders (SRBD)
  - ✓ Total: 155 (* 2021.01 ~ 2022.12)
  - ✓ 113 male & 42 female

- Significant OSA:
  - ✓ Oxygen desaturation index (ODI) of > 10 per hour

Methods & Statistics

- Polysomnography
- Echocardiography

- Purified exosomes of patients
  - ✓ Incubated in HL-1 cells.
  - ✓ mRNA expression
  - ✓ Inflammatory cytokines, gap junction
    - TNF-α
    - HIF-1α
    - IL-1 β
    - IL-6
    - TGF-β
    - GJA1 * Connexin 40/43

Methods & Statistics

Male

Female

- **Group:**
  - ✓ Control (ODI<10, AF-)
  - ✓ OSA only (ODI≥10)
  - ✓ OSA+AF (ODI≥10, AF+)

- **Method**
  - ✓ qPCR

- **Statistics**
  - ✓ One way ANOVA
  - ✓ Kruskal-Wallis H test
  - ✓ T TEST
  - ✓ Mann-Whitney U

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Baseline

PSG

ECHO

- **Cardiac remodeling: ♂ vs. ♀**
  - ✓ **Control**
    - **LVEDV: ♂ > ♀**
  - ✓ **OSA (+)**
    - **LVEDV: ♂ > ♀**
    - **Ao: ♂ > ♀**
    - **E/e': ♂ < ♀:**

Variable	Control (28)			OSAS only (103)		
	Male (n = 13)	Female (n = 15)	*P*-value	Male (n = 78)	Female (n = 25)	*P*-value
Age	50.0 (9.9)	56.2 (9.2)	0.096	51.8 (10.4)	62.0 (7.9)	<0.01
BMI					25.2 (3.8)	0.111
HTN (%)					10 (40.0)	0.639
DM (%)					3 (12.0)	0.398
HF (%)					0	-
AF (%)					0	-
CAD (%)					1 (4.0)	0.570
Stroke (%)					0	0.570
PSG data						
ESS					.0 (5.5-15.0)	0.649
AHI_{TST}					.0 (22.2-47.4)	0.142
AHI_{REM}					.8 (33.1-63.3)	0.664
AHI_{NREM}					.6 (21.3-44.4)	0.067
ODI_{TST}					.6 (14.7-34.0)	0.247
ODI_{REM}					.6 (13.9-55.3)	0.601
ODI_{NREM}					.8 (10.3-30.3)	0.229
Lowest SpO2					.0 (74.2-86.7)	0.200
Mean SpO2	94.6 (93.4-95.7)	95.0 (93.3-96.0)	0.856	93.8 (92.3-95.0)	93.7 (92.2-94.7)	0.648
SpO2<90%	1.3 (0.2-7.5)	2.1 (0.1-5.8)	0.964	5.9 (2.0-18.5)	6.0 (2.4-11.6)	0.620
Echocardiography						
AO	33.3 (5.2)	30.33 (3.7)	0.139	33.5 (3.5)	29.8 (2.7)	<0.01
LA	36.4 (3.5)	32.5 (6.6)	0.113	36.0 (4.7)	35.6 (3.6)	0.683
IVS	11.4 (0.8)	10.6 (1.4)	0.183	11.6 (1.8)	11.2 (1.4)	0.374
LVPW	8.7 (0.6)	9.3 (1.7)	0.324	9.3 (1.5)	8.9 (1.4)	0.284
LVEDV	119.6 (21.6)	95.6 (18.7)	0.014	114.5 (27.8)	101.0 (54.1)	0.038
LVESV	33.2 (8.0)	27.2 (6.5)	0.077	36.6 (19.0)	28.8 (10.0)	0.056
LVEF	72.33 (4.1)	70.8 (2.6)	0.323	68.3 (7.8)	71.6 (4.7)	0.054
E/e'	6.6 (2.2)	10.2 (4.5)	0.120	7.7 (2.1)	9.9 (3.2)	0.010

	Variable	Male (110) OSAS with AF (n = 19)	Male (110) OSAS only (n = 78)	Male (110) Control (n = 13)	P-value	Female (44) OSAS with AF (n = 4)	Female (44) OSAS only (n = 25)	Female (44) Control (n = 15)	P-value
Baseline	Age	60.5 (9.5)[b]	51.8 (10.4)[a]	50.0 (9.9)[a]	0.003	65.5 (11.1)	62.0 (7.9)	56.2 (9.92)	0.069
	BMI	26.7 (3.6)[b]	26.6 (3.1)[b]	23.6 (2.6)[a]					
	HTN (%)	9 (47.4)	27 (34.6)	4 (30.8)					
	DM (%)	3 (15.8)	5 (6.4)	1 (7.7)					
	HF (%)	3 (15.8)	0	0					
	AF (%)	19 (100)	0	0					
	CAD (%)	2 (10.5)	2 (2.6)	0					
	Stroke (%)	2 (10.5)	4 (5.1)	0					
PSG	PSG data								
	ESS	8.0 (4.0-11.0)	9.0 (6.0-12.0)	9.0 (5.0-11.0)					
	AHI_{TST}	39.5 (26.0-63.0)[b]	42.3 (25.7-58.3)[b]	7.6 (3.4-10.6)[a]					
	AHI_{REM}	45.0 (37.7-58.5)[b]	48.0 (31.0-62.9)[b]	13.5 (5.7-19.8)[a]					
	AHI_{NREM}	34.7 (23.3-63.9)[b]	44.1 (23.2-58.4)[b]	6.3 (3.2-8.7)[a]					
	ODI_{TST}	29.9 (13.4-62.0)[b]	27.5 (13.0-45.1)[b]	4.6 (1.1-6.8)[a]					
	ODI_{REM}	39.1 (22.7-55.9)[b]	41.1 (18.9-55.0)[b]	7.3 (1.7-12.8)[a]					
	ODI_{NREM}	31.2 (11.6-61.8)[b]	29.3 (11.2-44.1)[b]	4.5 (1.8-6.4)[a]					
	Lowest SpO2	78.0 (62.5-87.0)[b]	79.0 (73.0-84.0)[b]	89 (85-91.5)[a]					
	Mean SpO2	92.2 (91.0-94.9)[b]	93.8 (92.3-95.0)[ab]	94.6 (93.4-95.7)[a]					
	SpO2<90%	11.6 (4.2-26.4)	5.9 (2.0-18.5)	1.30 (0.25-7.5)	0.054	5.2 (2.9-6.3)	6.0 (2.4-11.6)	2.1 (0.1-5.8)	0.162
ECHO	Echocardiography								
	AO	34.0 (4.1)	33.5 (3.5)	33.3 (5.2)	0.881	30.5 (4.7)	29.8 (2.7)	30.3 (3.7)	0.874
	LA	40.0 (6.3)[b]	36.0 (4.7)[a]	36.4 (3.5)[ab]	0.011	42.0 (4.9)[b]	35.6 (3.6)[ab]	32.5 (6.5)[a]	0.005
	IVS	11.7 (2.8)	11.6 (1.8)	11.4 (0.8)	0.904	12.0 (1.4)	11.2 (1.4)	10.6 (1.4)	0.256
	LVPW	9.6 (2.1)	9.3 (1.5)	8.7 (0.6)	0.446	9.2 (0.9)	8.9 (1.4)	9.3 (1.7)	0.759
	LVEDV	112.4 (44.0)	114.5 (27.8)	119.6 (21.6)	0.851	91.0 (19.7)	101.0 (25.1)	95.6 (18.7)	0.636
	LVESV	43.7 (28.6)	36.6 (19.0)	33.2 (8.0)	0.332	34.7 (15.6)	28.8 (10.0)	27.2 (6.5)	0.423
	LVEF	64.0 (7.8)[b]	68.3 (7.8)[ab]	72.3 (4.1)[a]	0.027	63.7 (7.8)[b]	71.6 (4.7)[a]	70.8 (2.6)[a]	0.012
	E/e'	10.3 (3.5)[b]	7.7 (2.1)[a]	6.6 (2.2)[a]	0.001	10.9 (1.9)	9.9 (3.2)	10.2 (4.5)	0.906

- **OSA vs. OSA with AF**
  - ✓ **Male**
    - Age
    - LA
    - E/e'
  - ✓ **Female**
    - LVEF

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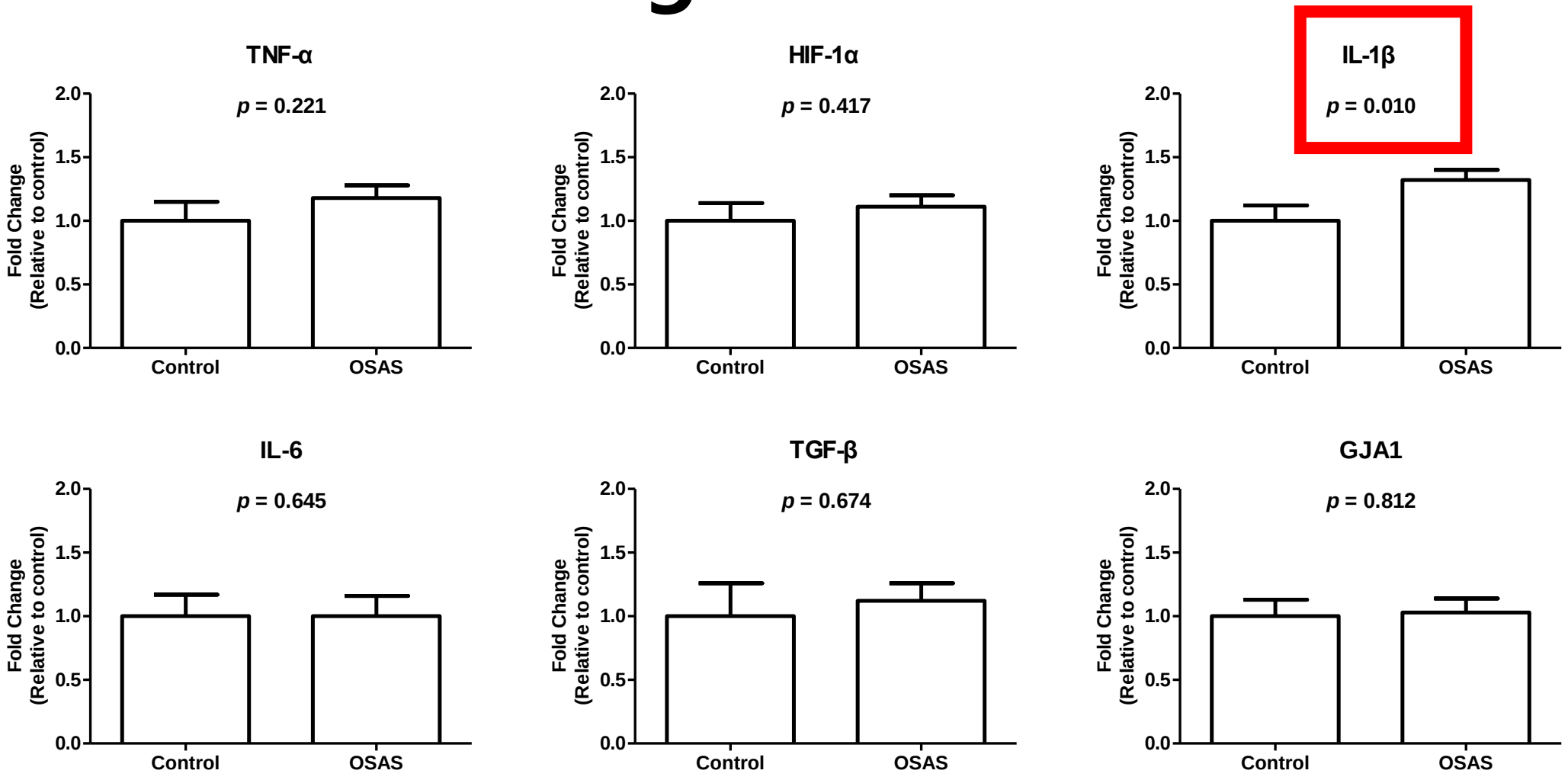
Male

Figure 1



IL-1 β, statistical significances

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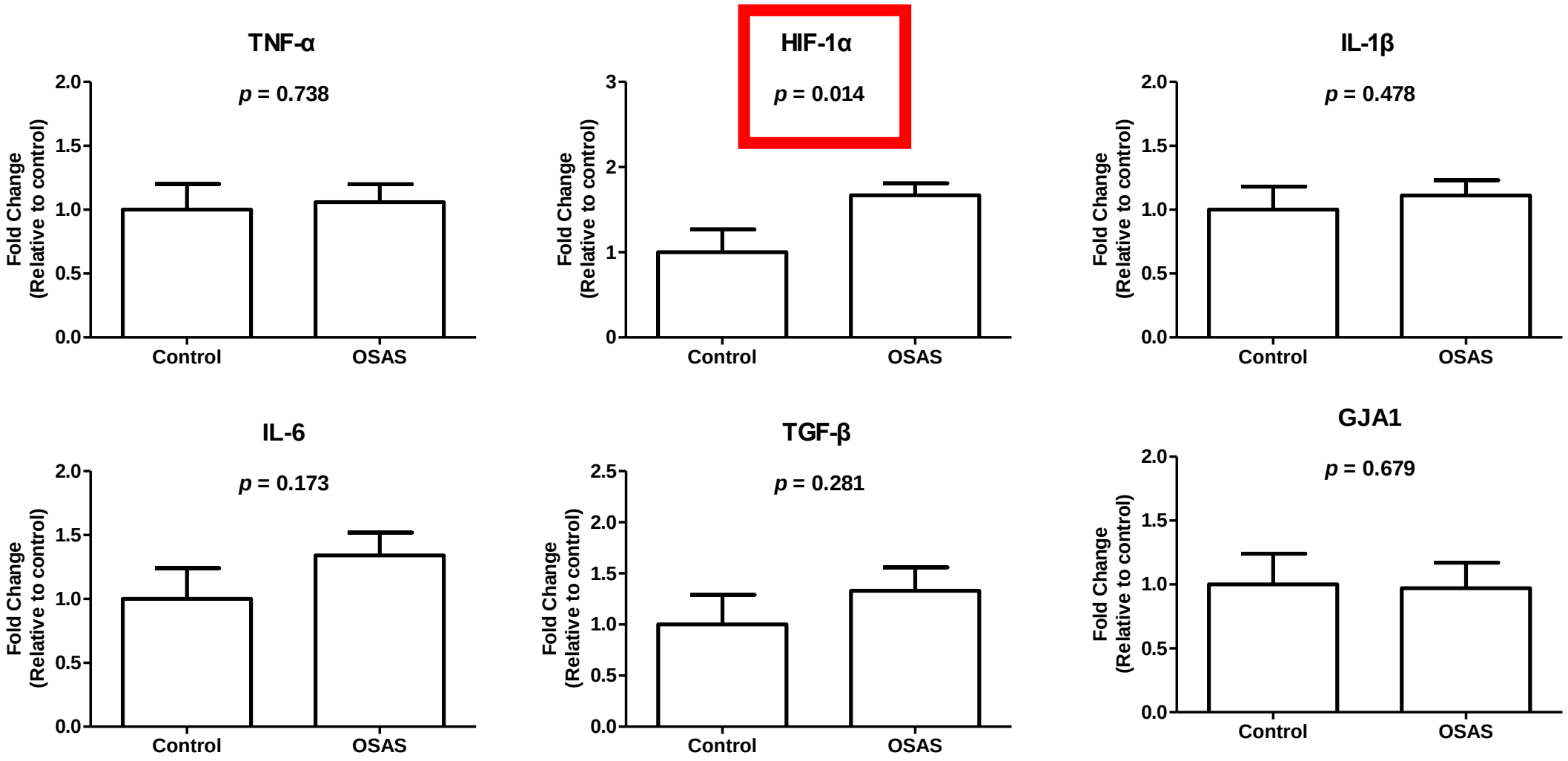
Female

Figure 2



HIF-1 α, statistical significance

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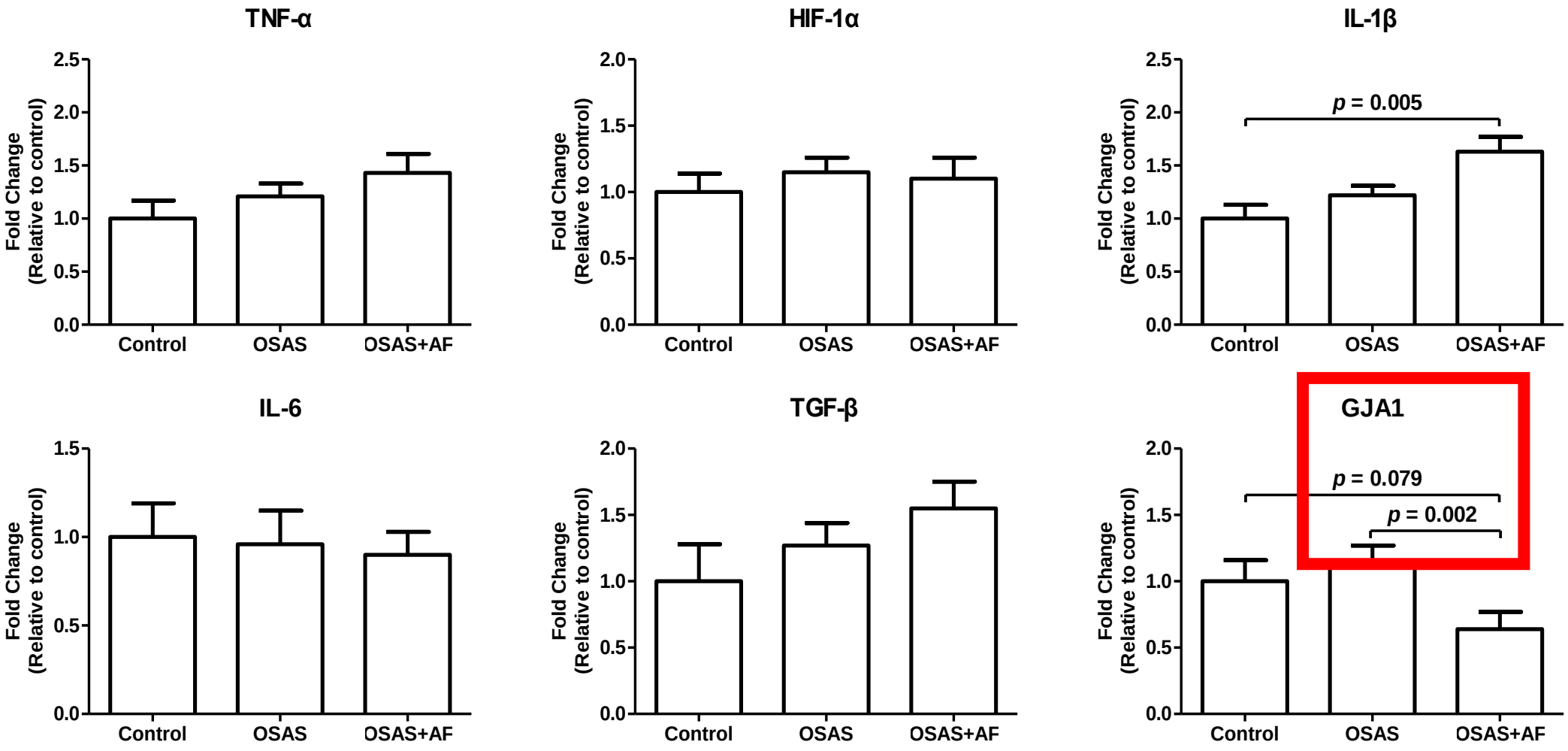
Male

Figure 3



GJA1, statistical significance

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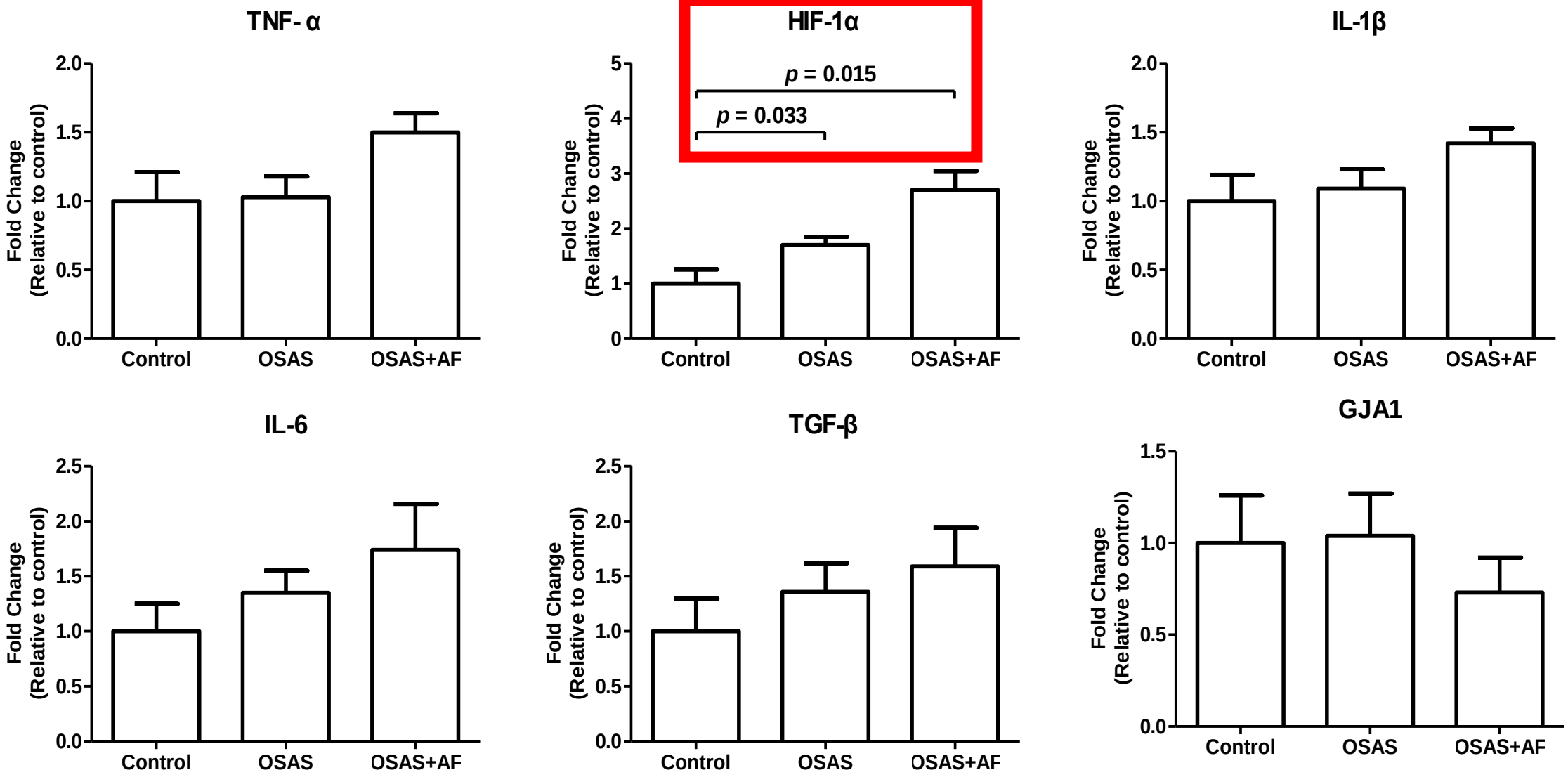
Figure 4

Female



HIF-1 α, higher expression, but no statistical significance

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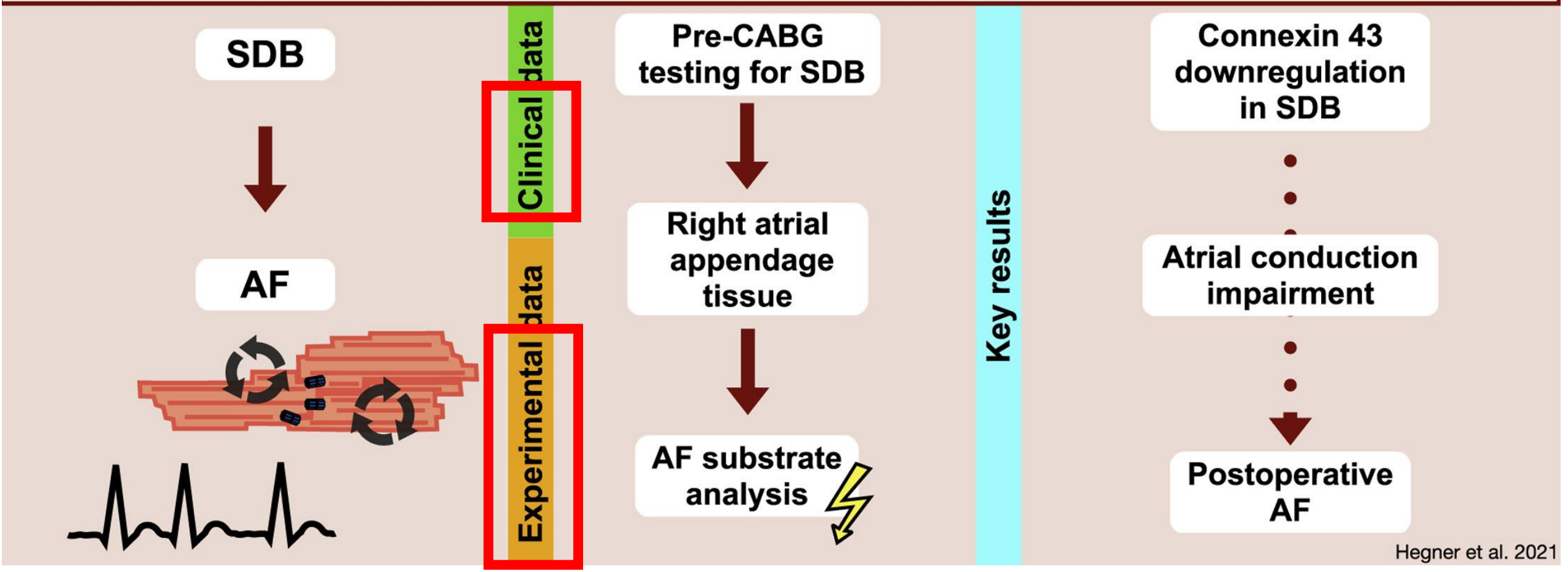
Sleep-disordered breathing is independently associated with reduced atrial connexin 43 expression



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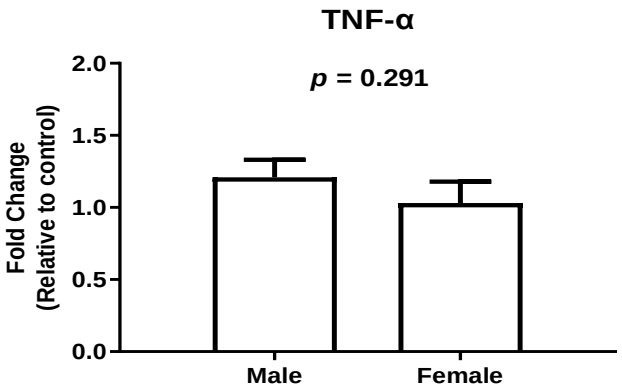
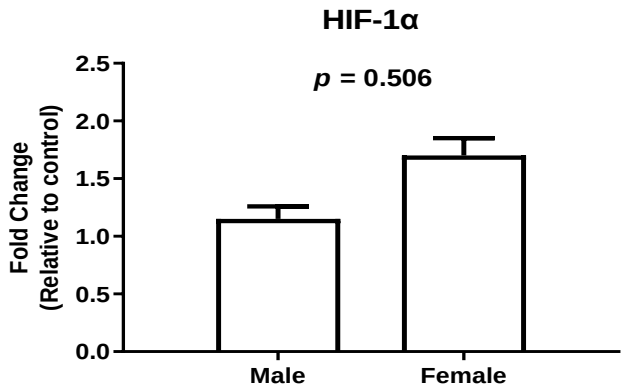
Conclusions

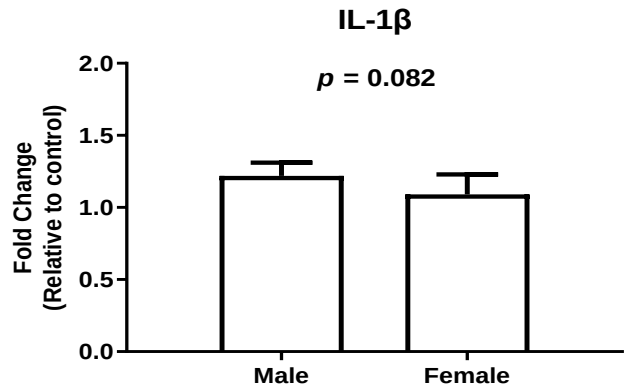
- For patients diagnosed with OSA, there are differences in **cardiac remodeling** in terms of different sexes.
- The expression of **GJA1** may offer a plausible mechanism for AF development in **male** patients.
- Further in vivo studies on the **mechanisms of AF development** in different sexes may be carried out.

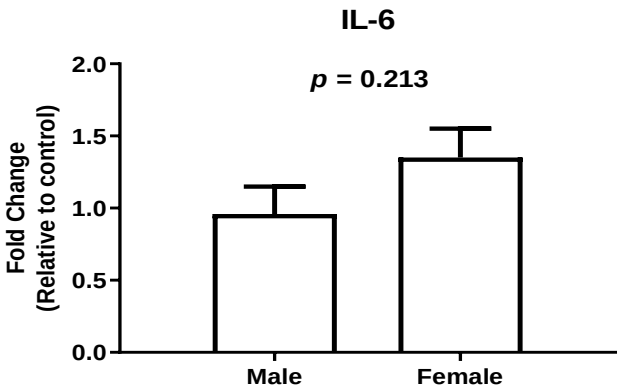
Q & A session

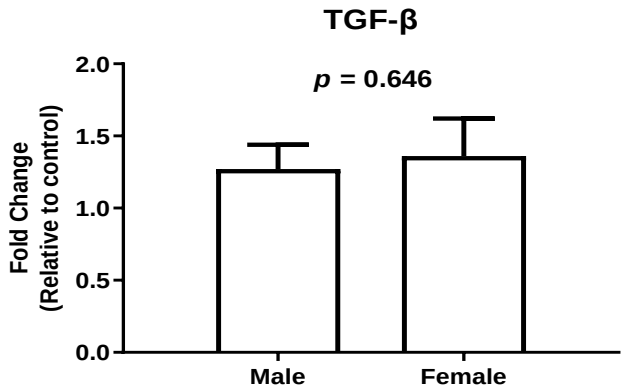
Discussion

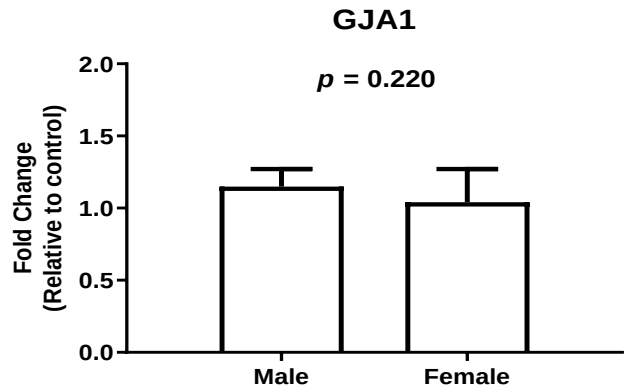








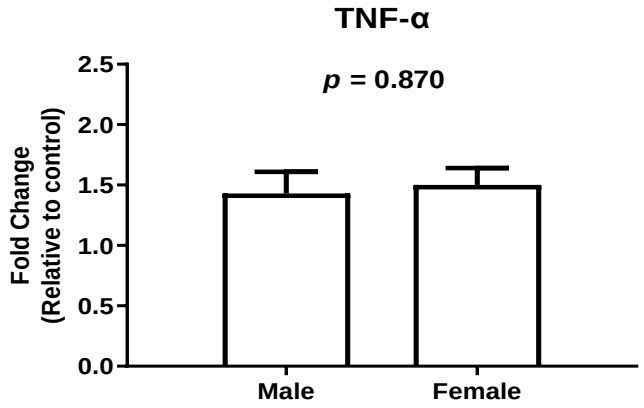


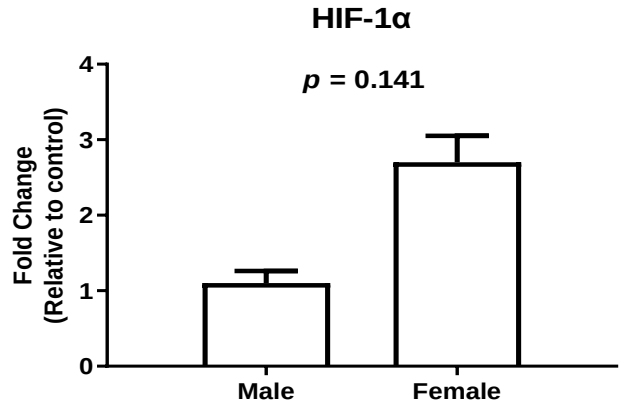


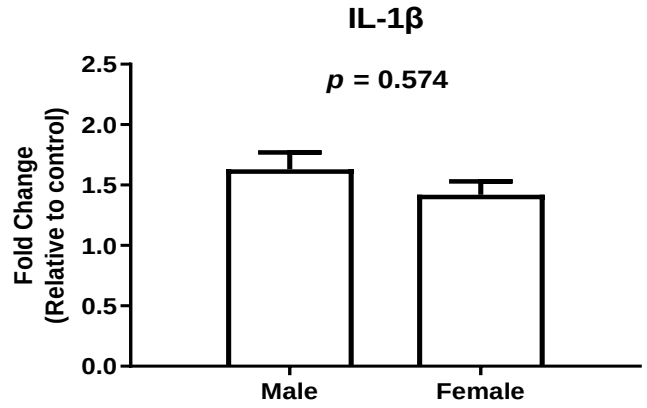
- OSA (+), male vs. female
- No statistical significance

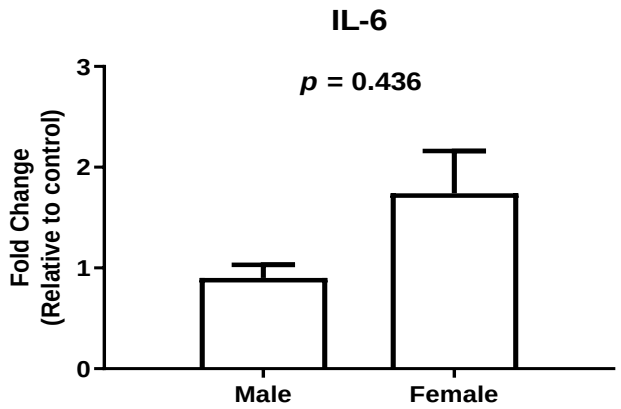
- ♂ :19 OSA + AF, 78 OSA only
- ♀: 4 OSA + AF, 25 OSA only

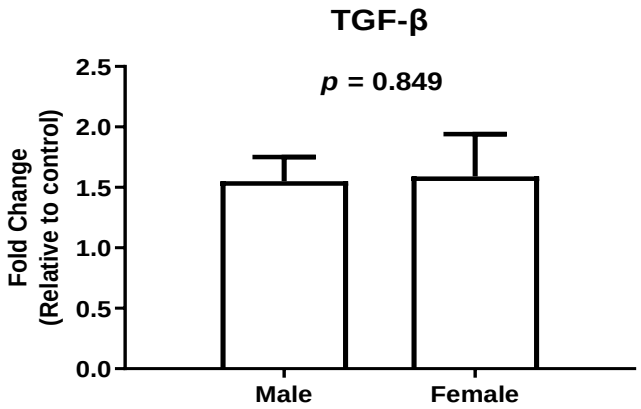
Discussion

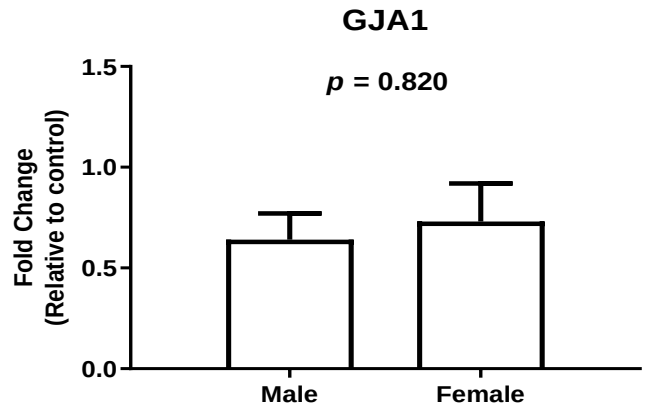












- OSA (+), AF (+) , male vs. female
- No statistical significance

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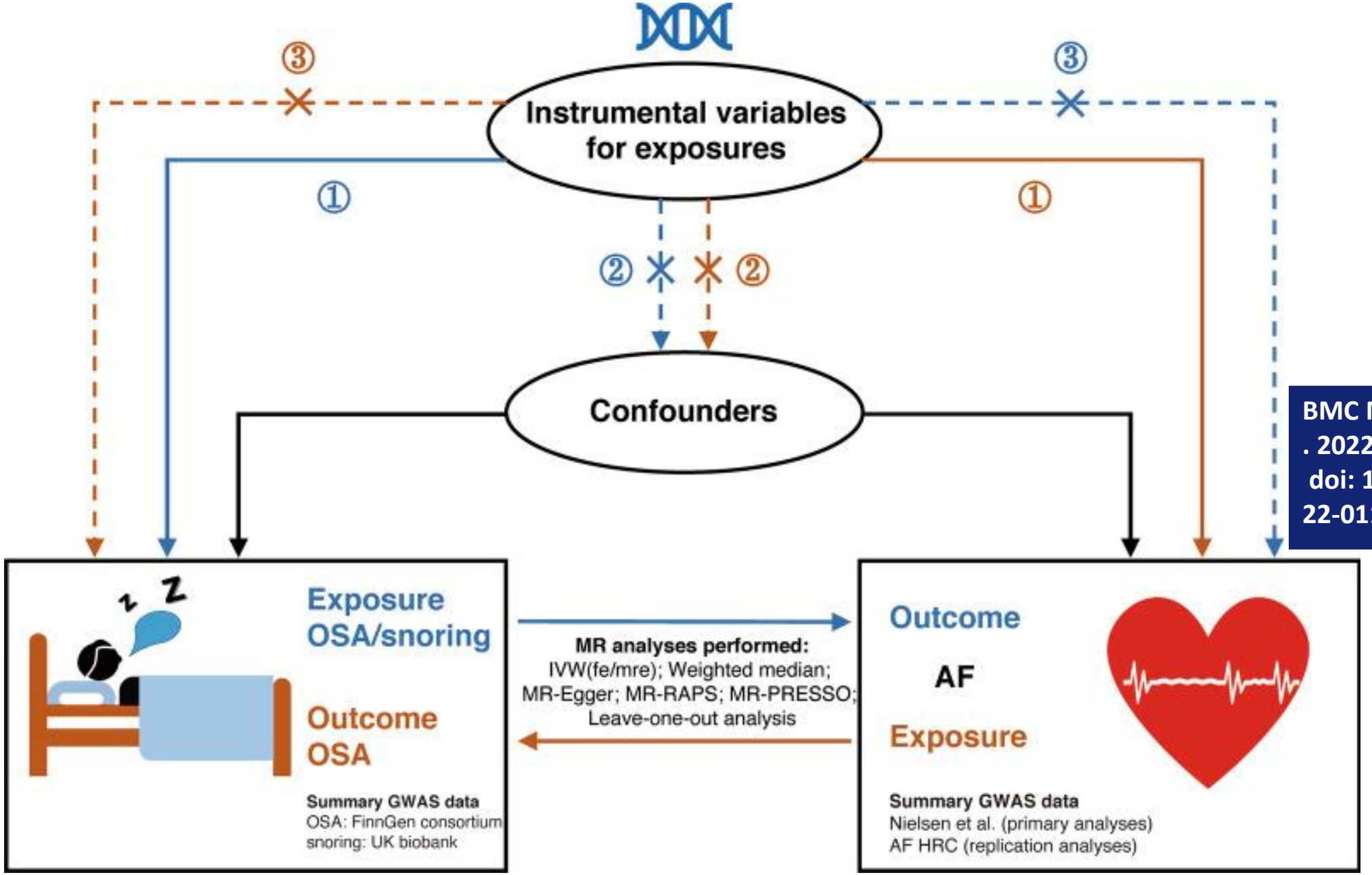

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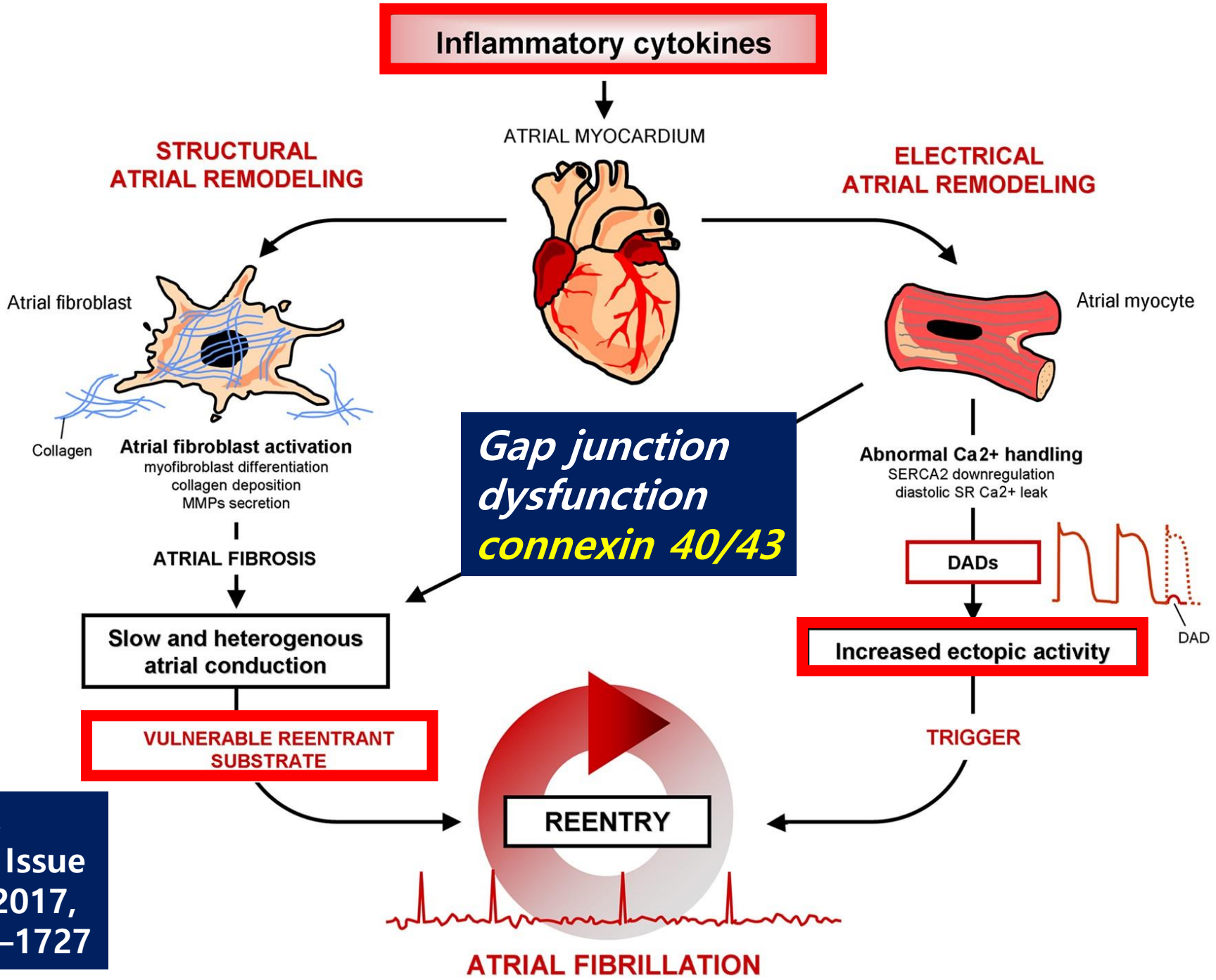

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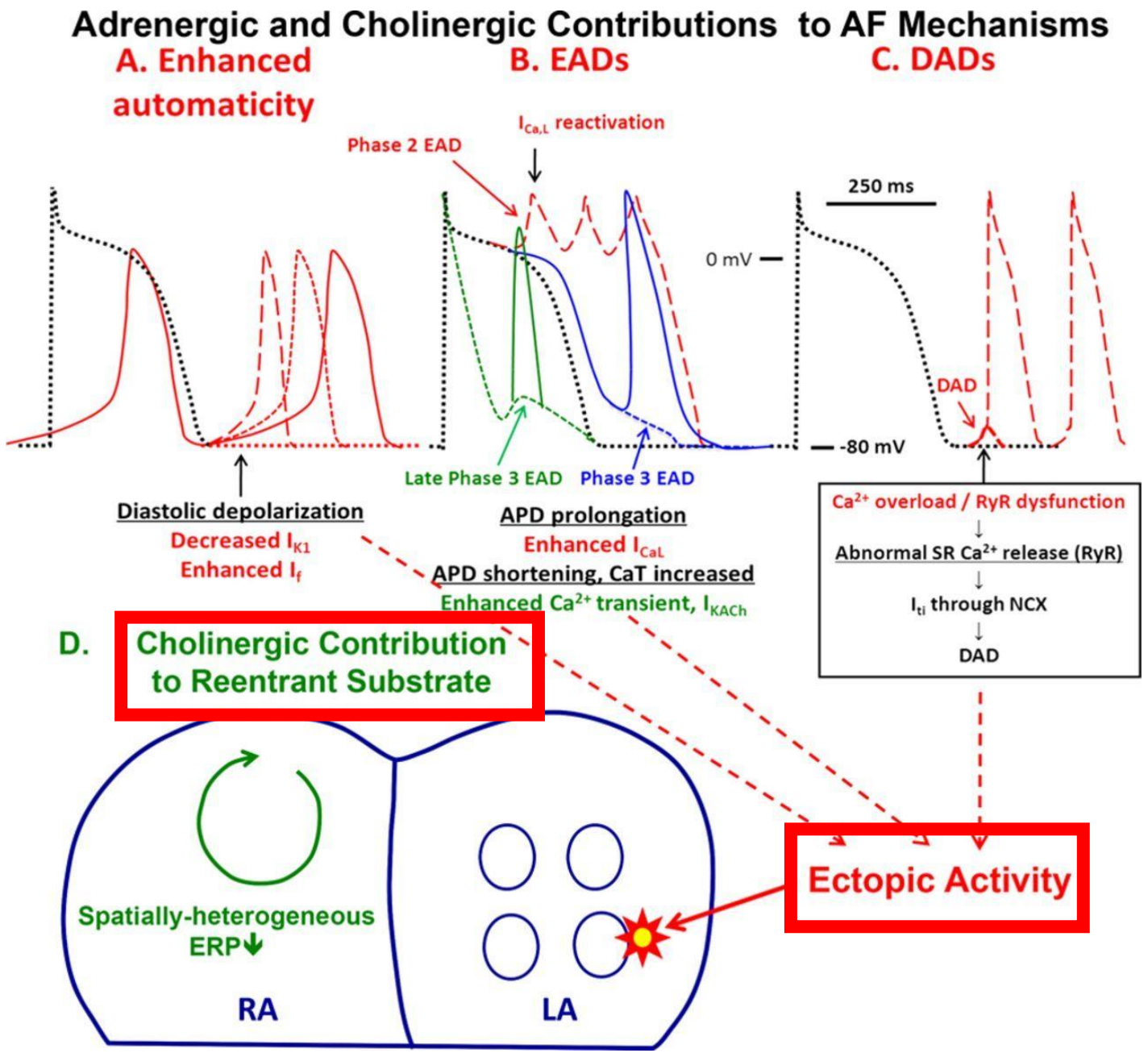

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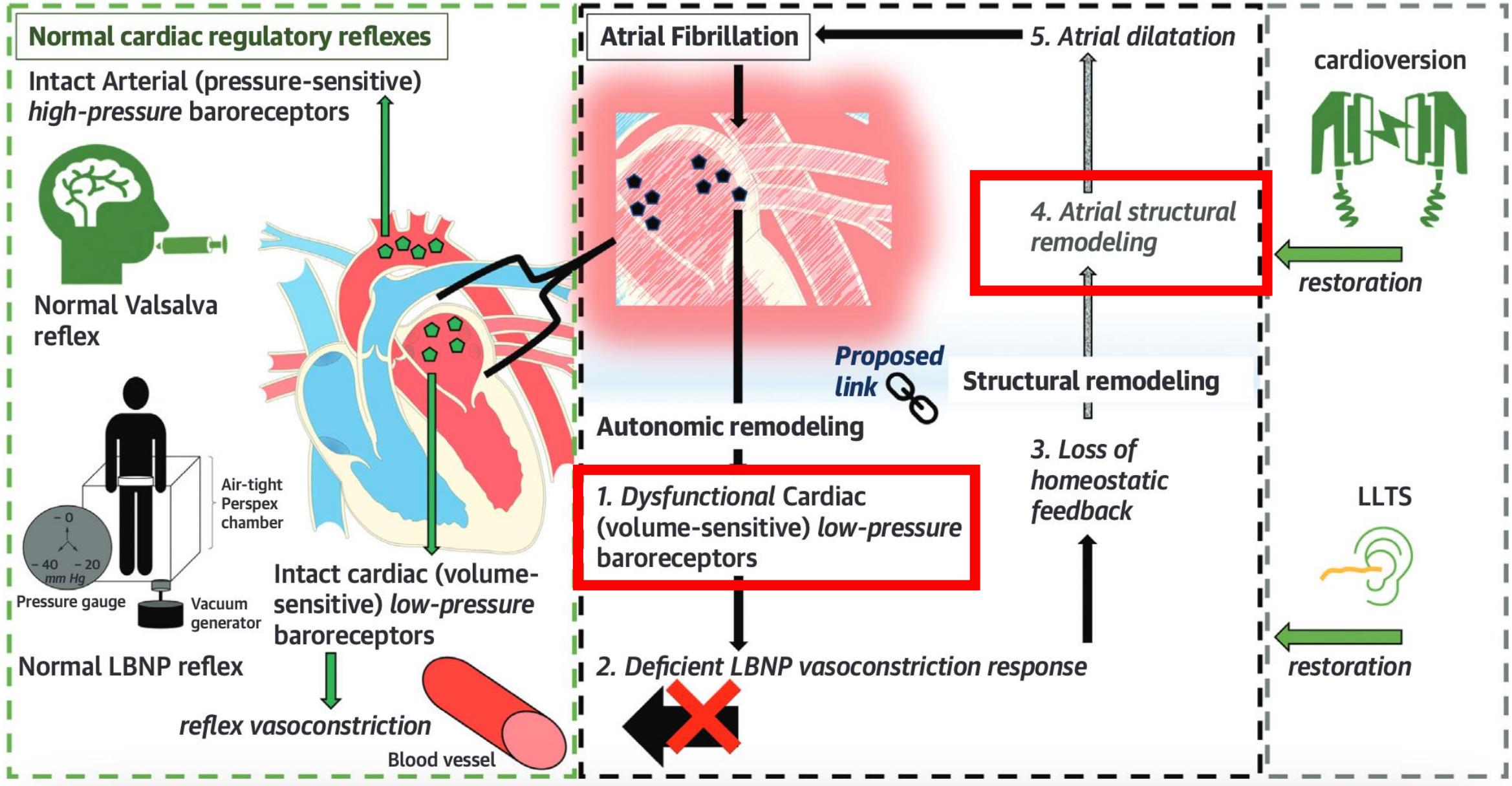

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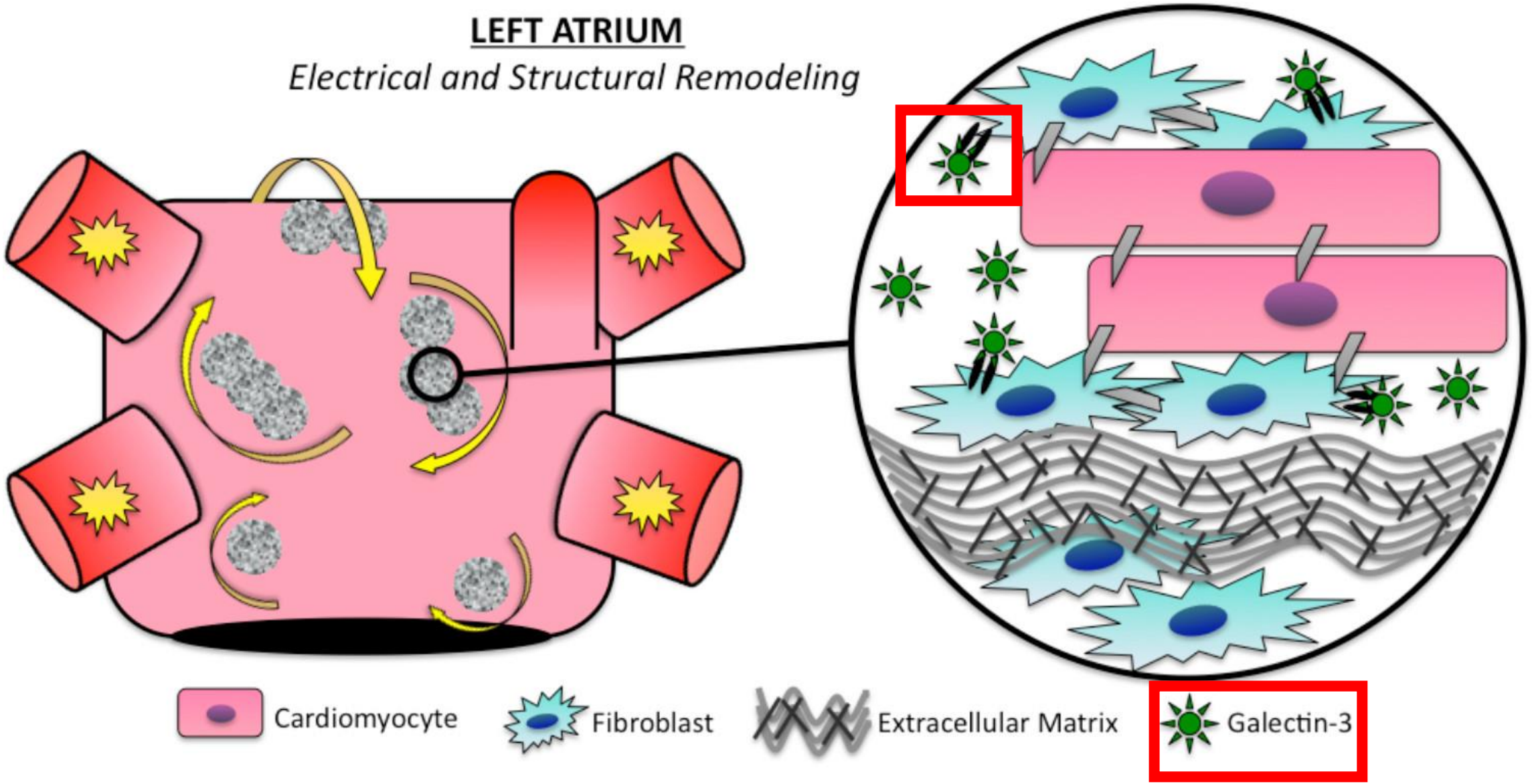

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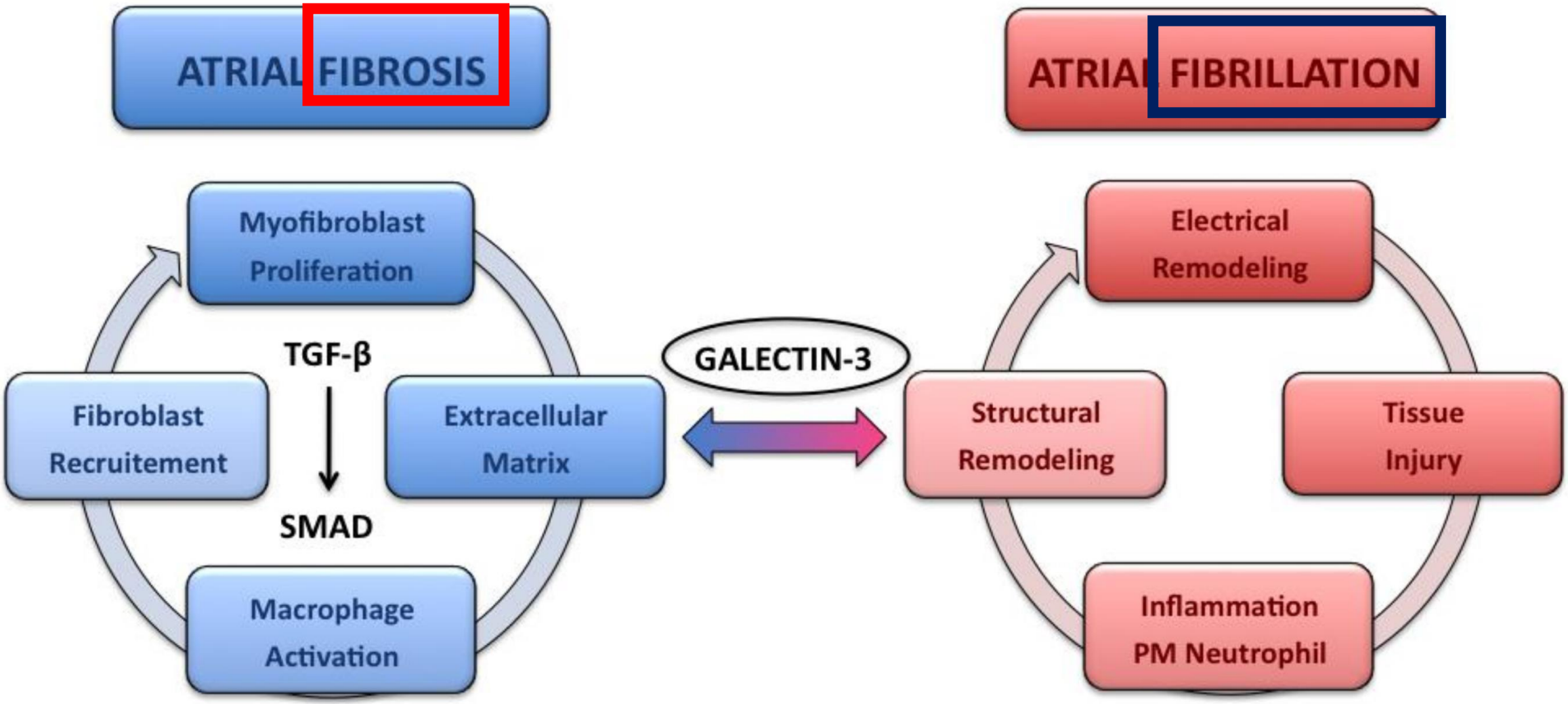

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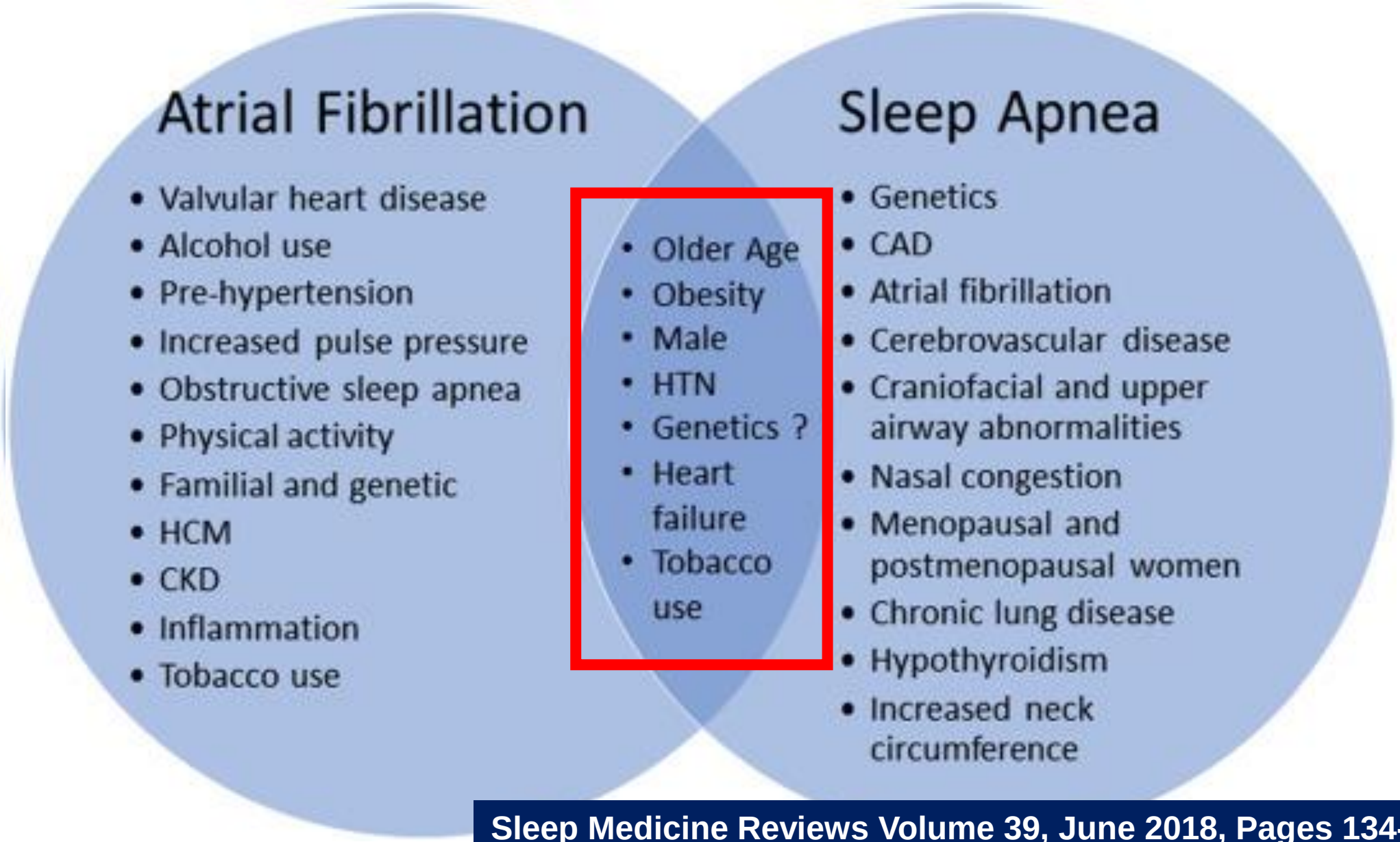

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