Migraine

Study Details	Patients	Interventions	Outcome measures	Effect size	Comments
Author & Year: D'Souza et al, 2008[182] **Study design:** RCT **Comparison:** Written emotional disclosure vs neutral writing control **Setting:** University psychology department **Duration of follow-up:** 3 months	**Patient group:** Undergraduate psychology students with migraine or tension type headache (TTH). **Inclusion criteria:** Fulfilled IHS criteria for either migraine or TTH. Headaches at least twice per week that were of moderate or severe intensity OR migraine headache at least once a month. **Exclusion criteria:** Headaches suspected to be due to neurological disease, alcohol abuse or a primary medical disorder or those currently in psychotherapy or counselling. **All patients** **N:** 141 (51 TTH, 90 migraine) **Drop outs:** 6 **Tension Type Headache** **Age (mean, SD):** 20.27 (2.30) **M:F (n, %):** 42:9 (82.4: 17.6) **Group 1 – Written emotional disclosure (WED)** **N:** 17 **Age (mean):** NR	**Group 1 Written emotional disclosure (WED)** 4 sessions over 2 weeks (four 20 min sessions over 2 consecutive weeks). Standard instructions to write about 'a trauma or upheaval or stressful experience that you may be experiencing right now or that you experienced at some other time in your life', particularly ' the most stressful that you have experienced and is the most significant to you' and 'ideally one that you have not talked about in detail with others'. Participants were encouraged to write about the facts as well as their deepest feelings and to try to write about the same event for all four writing days. Finally they were encouraged to 'tell a story' and consider writing about how the event has affected their relationships, health or headaches. Writings were left with the research team at the end of the session. Not encouraged to practice at home. **Group 2 neutral writing control** 4 sessions over 2 weeks (four 20 min sessions over 2 consecutive weeks). Engaged in time management writing to control for expectations, number of sessions, effort and attention from	**Change in patient-reported headache frequency** (in last month (Mean SD)) Follow-up 3months (adjusted follow up adjusted for baseline value) **Patient-reported headache intensity** (0-10 scale 10=bad, mean (SD)) Follow-up 3months (adjusted follow up adjusted for baseline value)	**Tension headache** **Group1:** 9.94 (SD 7.22) at baseline, 12.24 (SD 7.90) at follow-up, 12.56 (SEM 1.60) adjusted follow-up **Group 2:** 9.65 (SD 6.64) at baseline, 11.24 (SD 9.01) at follow-up, 11.74 (SEM 1.60) adjusted follow-up **Migraine** **Group1:** 9.65 (SD 6.46) at baseline, 9.00 (SD 5.81) at follow-up, 9.37 (SEM 0.93) adjusted follow-up **Group 2**: 11.77 (SD 7.58) at baseline, 8.97 (SD 6.14) at follow-up, 8.35 (SEM 0.94) adjusted follow-up **Tension headache** **Group1:** 5.47 (SD1.81) at baseline, 5.00 (SD 1.62) at follow-up, 5.00 (SEM 0.44) adjusted follow-up **Group 2:** 5.43 (SD 1.79) at baseline, 4.71 (SD 1.80) at follow-up, 4.73 (SEM 0.44) adjusted follow-up **Migraine group** **Group1:** 6.39 (SD 1.52) at	**Funding:** Arthritis Foundation and grant from National Institute of Health **Limitations:** Blinding unclear Students were given course credit or money for participating. Migraine group headache frequency not comparable at baseline. N completing 3 month follow-up unclear. **Additional outcomes:** Mood immediately following intervention. Physical symptoms. **Notes:**

Study Details	Patients	Interventions	Outcome measures	Effect size	Comments
	Drop outs: 0 **Group 2 - neutral writing control** **N:** 17 **Age (mean):** NR **Drop outs:**1 **Group 3-relaxation training** N: **17** **Migraine** **Age (mean):** 21.44 (SD 5.47) **M:F (n, %):** 80:10 (88.9: 11.1) **Group 1 – Written emotional disclosure (WED)** **N:** 31 **Age (mean):** NR **Drop outs:** 3 **Group 2 - neutral writing control** **N:** 31 **Age (mean):** Not Reported **Drop outs:** 1 **Group 3- relaxation training** N: **28**	laboratory personnel received by both active groups. Participants wrote about their activities for the past week (session 1) and past 24h (session 2) and their planned activities for the next 24h (session 3) and next week (session 4). Instructions asked participants to write only about their actions but to refrain from writing about their feelings or opinions. Not encouraged to practice at home. Group 3- relaxation training results not reported in this table. **All patients** Completed prospectively a brief diary each evening during the follow-up period, recording the presence and severity of headaches each day.		baseline, 5.23 (SD 2.28) at follow-up, 5.25 (SEM 0.34) adjusted follow-up **Group 2:** 6.35 (SD 1.14) at baseline, 5.55 (SD 1.69) at follow-up, 5.60 (SEM 0.34) adjusted follow-up	Randomisation: random numbers table in blocks of 6; performed separately for the tension and migraine headache samples. ITT with last observation carried forward.
			Headache specific QoL (MIDAS) Follow-up 3months (adjusted follow up adjusted for baseline value)	**Tension headache** **Group1:** 8.24 (SD 8.84) at baseline, 8.35 (SD 8.89) at follow-up, 9.23 (SEM 1.43) adjusted follow-up **Group 2:** 9.24 (SD 6.53) at baseline, 7.29 (SD 7.82) at follow-up, 7.73 (SEM 1.42) adjusted follow-up **Migraine** **Group1:** 13.35 (SD 11.83) at baseline,9.87 (SD 8.79) at follow-up, 10.05 (SEM 1.62) adjusted follow-up **Group 2:** 15.35 (SD 12.25) at baseline, 10.13 (SD 11.49) at follow-up, 9.13 (SEM 1.63) adjusted follow-up	

Abbreviations: NR=not reported, M/F=male/female, N= number of patients, SD=Standard deviation, SE=Standard error, ITT=Intention to treat analysis, CI=confidence interval, TTH=tension type headache, WED=written emotional disclosure

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Author & Year: Richter et al, 1986[666] **Study design:** RCT **Comparison:** Relaxation training / cognitive coping vs placebo **Setting:** Children's Hospital, Canada **Duration of follow-up:** 16 weeks (4 week baseline, 6 week treatment, 4 weeks post-treatment, 4 weeks follow-up)	**Patient group:** Children and adolescents with migraine **Inclusion criteria:** Age 9-18 years; Confirmation of the diagnosis of classical or common migraine by a project neurologist using the diagnostic criteria of intermittent paroxysmal headache and any 2 of the following 4 symptoms: throbbing pain, scotomata or related neurologic phenomena, nausea and/or vomiting and a positive family history; Minimum headache history of 3 months; Average frequency of once per week; No new prophylactic medication within the previous 2 months; Minimum IQ of 80 on the PPVT. **Exclusion criteria:** Allergic; purely dietary or menstrual headache; Unstable emotional or medical problems likely to require other medications. **All patients** **N:** 51 (17 M, 34 F), 42 evaluable **Age (mean):** 12.87 **Drop outs:** 8, and 1 child failed	**Group 1 – relaxation training** Closely followed the procedure developed by Cautela and Groden for children. Subjects were taught the sequential tensing and relaxing of large muscle groups and the use of deep breathing to achieve total body relaxation. They were then taught sequential relaxation without tensing, differential relaxation, self-cueing and 'mini' relaxation. They were instructed to practice daily and to use their relaxation skills as soon as they noticed stress levels rising, if they were involved in a stress-producing situation, or at the onset of a headache. **Group 2 - cognitive coping** This programme, called 'thinking straight' was developed by the authors as a downward extension of Holroyd and Andrasik's cognitive self-control programme and Bakal's cognitive-behavioural treatment. It emphasised altering maladaptive thought processes which mediate unpleasant emotions and biochemical concomitants which may precipitate the headache process. The programme used elements of cognitive restructuring, the cognitive control of pain, fantasy, simple problem solving and stress-inoculation training. Children were taught to monitor their stress reactions on a daily basis, to record and restructure thought processes, and to note the emotional correlates of their cognitive patterns. They were instructed to use the procedures in all stress-provoking situations as well as for the control of headache pain. Personalised cards containing coping statements were prepared for each subject. **Group 3 - placebo**	**Change in patient-reported headache frequency** baseline and final values, mean (SD)) Follow up at 14 weeks **Change in patient-reported headache intensity** (baseline and final values, mean (SD)) Peak intensity on a scale of 0-5 Follow up at 14 weeks	**Group1:** Baseline 9.03 (8.05) Follow-up 2.91 (3.40) **Group 2:** Baseline 8.14 (7.82) Follow-up 2.52 (2.94) **Group 3:** Baseline 7.26 (6.12) Follow-up 4.68 (5.83) **Group1:** Baseline 3.60 (1.08) Follow-up 2.08 (1.73) **Group 2:** Baseline 3.37 (0.77) Follow-up 1.96 (1.23) **Group 3:** Baseline 3.58 (0.76) Follow-up 2.02 (1.39)	**Funding:** Ontario Ministry of Health and the Ontario Ministry of Community and Social Services **Limitations:** Randomisation method unclear **Additional outcomes:** Headache duration Headache index **Notes:** Available case analysis

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	to monitor adequately during follow-up **Group 1 – relaxation training** **N:** 15 **Age (mean):** NR **Drop outs:** not stated **Group 2 – cognitive coping** **N:** 15 **Age (mean):** NR **Drop outs:** NR **Group 3 – placebo** **N:** 12 **Age (mean):** NR **Drop outs:** NR	Attention-control or non-specific condition, 'stress reduction training'. Structurally identical to the experimental groups, i.e. it provided information on the causes of migraine, a credible treatment rationale, expectations for improvement, a set of sham 'coping skills' and daily homework. Subjects were taught to recognise and label their emotions, to relate them to the situation in which they occurred, and to discuss their feelings daily with a friend o parent. Considered a credible placebo, not unlike non-directive psychotherapy with no theoretically active treatment components. **All patients** Baseline phase: patients were taught to monitor headache activity 4 times daily using a headache diary. All subjects received 1hour of individual therapy weekly which followed detailed treatment manuals to standardised procedures. In the first session all groups were given information about the nature of migraine, the role of stress and other triggers, and the specific treatment rationale was explained. The 3 rationales were identical except for slight differences in explaining the respective mechanisms of action. All treatments were presented as stress-coping techniques which could be used to reduce tension and anxiety and thereby short-circuit the migraine process.			

Abbreviations: NR=not reported, M/F=male/female, N= number of patients, SD=Standard deviation, SE=Standard error, ITT=Intention to treat analysis, CI=confidence interval

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
Author & Year: Varkey et al, 2011[819] **Study design:** RCT **Comparison:** Exercise vs topiramate vs relaxation **Setting:** Specialist headache clinic, Sweden **Duration of follow-up:** 3 and 6 months after treatment.	**Patient group:** Patients with migraine recruited from newspaper adverts and headache clinic. **Inclusion criteria:** Aged 18-65; migraine with or without aura according to ICHD-II criteria; frequency of 2-8 attacks per month; had migraine for at least 1 year before participating in the study and before the age of 50. **Exclusion criteria:** Interval headaches not distinguishable from migraine; medication overuse headache; regular exercise (once or more per week during the 12 weeks prior to the study); earlier practice of relaxation, pregnancy, breastfeeding or use of daily migraine prophylaxis in the 12 weeks prior to the study; inability to understand Swedish; use of antipsychotic or antidepressive medication in the 12 weeks prior to the study; drug or alcohol abuse;, topiramate intolerance. **All patients** **N:** 91 **Age (mean):** 44.4 (11.3) **Drop outs**: 44	**Group 1 - Exercise** Trained with a registered physiotherapist for 40 minutes three times/ week. Exercise programme based on indoor cycling and the rate of perceived exertion was used to set the intensity of the exercise programme. Training session included 15 min warm up, 20 min exercise programme, 5 min cool down. There was opportunity to discuss the exercise programme with the therapist after the session. If participant was absent they exercised at home or a local gym. All forms of continuous aerobic exercise were then accepted, participants instructed to reproduce same intensity and duration of exercise used in the programme. Participants who exercised 1/ week at clinic and >2/ week were considered adhering to treatment. **Group 2 - Topiramate** Visited neurologist before starting a course of topiramate. Dosage was increased by 25mg/week until the dosage	**Responder rate** (50% reduction in migraine attack frequency) at 3 months	**Group 1:** 9/30 **Group 2:** 8/31 **Group 3:** 7/30 **p value:** NR	**Funding:** Swedish research council, Gothenburg research and development council, Swedish association of physiotherapists, Renee Eander fund, Neurological research foundation, Olle Engkvists Byggmastare foundation, Glaxosmithkline, Astrazeneca. **Limitations:** Single blind (evaluator only). >10% dropped out of study at 3 month follow up, but similar in all groups. Unclear for how long patients trained with a physical therapist- reads as though only at the beginning then participant took control of exercise programme for at least 2 of the 3 sessions per week. Study based on a self selected sample. Patients who already undertook regular exercise were excluded. **Additional outcomes:** Body weight VO_2max Data at 6 months
			Change in patient-reported migraine days (n/month, least squares mean (SE)) **[SD] Change from baseline at 3 months	**Group 1:** -2.23 (0.55) **[3.01] **Group 2:** -2.08 (0.54) **[3.01] **Group 3:** -1.47 (0.55) **[3.01] **p value:** NR	
			Change in patient-reported migraine frequency (attacks†/month, least squares mean (SE)) **[SD] Change from baseline at 3 months	**Group 1:** -0.98 (0.58) **[1.53] **Group 2:** -0.68 (0.28) **[1.56] **Group 3:** -0.94 (0.28) **[1.53] **p value:** NR	
			Change in patient-reported migraine intensity (VAS 0-100, least squares mean (SE)) **[SD] Change from baseline at 3 months	**Group 1:** -7.1 (3.5) **[19.17] **Group 2:** -13.7 **[18.93] **Group 3:** -5.1 (3.5) **[19.17] **p value:** NR	
			Headache specific QoL Swedish version of	**Group 1:** 5.0 (2.3) **[12.60] **Group 2:** 2.4 (2.3)	

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Group 1 – Exercise **N:** 30 **Age (mean):** 47 (10.8) **Drop outs:** 8 at 3 months, 5 withdrew (1 lack of time, 4 non-compliance) 3 no data, 14 at 6 months. **M/F:** 5/ 25 **Disease duration (years):** 28.8 (11.0) **Migraine frequency (days/month):**7 (3.8) **Migraine frequency (attacks†/month):**4.3 (2.0) **Frequency of headache medication used (doses/month):** 6.9 (4.1) **Intensity of pain (median, IQR):** 50 (26-64) **MSQoL (median, IQR):** 60 (43-77) **Group 2 - topiramate** **N:** 31 **Age (mean):** 44.4 (9.2) **Drop outs: :** 11 at 3 months, 10 withdrew (7 refused drugs, 3 adverse events) 1 no data, 14 at 6 months. **M/F:**2/29 **Disease duration (years):** 25.1 (11.4) **Migraine frequency (days):** 7.5 (3.9) **Migraine frequency (attacks):**3.6 (1.6)	reached the highest dose that the individual could tolerate, maximum of 200mg/day. Allowed to call neurologist any time of day during the treatment period to book a scheduled visit if needed. At least 1 follow up visit was scheduled. Adherence defined as using the medicine for > 2 months in accordance with prescription and was measured using self reports. **Group 3 – Relaxation** Scheduled individual appointment with a registered physiotherapist once a week. The programme was based on common forms of relaxation, breathing and stress-management techniques (described by Larsson and Andrasik) and includes a series of 6 exercises, each of which is based on the one before. Each lasted between 5-20minutes and verbal and written information was given before the introduction of a new relaxation exercise. After each session there was an opportunity to discuss their progress with the	the migraine specific QoL questionnaire [Scale 1- 100] least squares mean (SE) **[SD] **Use of acute pharmacological treatment** (doses/ month) least squares mean (SE) **[SD] **Incidence of adverse events (%)** **NB none were serious**	**[12.81] **Group 3:** 3.1 (2.4) **[13.15] **p value:** NR **Group 1:** -2.72 (0.55) **[3.01] **Group 2:** -2.71 (0.54) **[3.01] **Group 3: -**2.84 (0.54) **[2.96] **p value:** NR **Group1:** 0/30 **Group 2:** 3/31* **Group 3:** 0/30 **p value:** NR	**Notes:** ANCOVA used to adjust for baseline differences (these results are reported) ** SD calculated by NCGC ITT analysis undertaken with last observation carried forward for missing data. *3 patients state AE as reason for withdrawal. 8 patients reported AEs in total. No serious AEs reported. Participants randomised after the baseline period. Randomisation by independent person by a lottery method. †Migraine attack defined as concomitant days with migraine headache and distinct attacks were counted if separated by ≥24 hours.

Study details	Patients	Interventions	Outcome measures	Effect size	Comments
	Frequency of headache medication used (doses): 7.1 (5.3) **Intensity of pain (VAS) (median, IQR):** 40 (29-58) **MSQoL (median, IQR):** 60 (48-73) **Group 3 – relaxation** (N=30) **N:** 30 **Age (mean):** 41.5 (11.4) **Drop outs:** 7 at 3 months, 4 withdrew (2 not satisfied, 1 lack of time, 1 unexplained) 1 no data, 16 at 6 months. **M/F:** 2/28 **Disease duration (years):** 22.2 (11.8) **Migraine frequency (days/month):**7.6 (3.8) **Migraine frequency (attacks†/month):**4.2 (1.6) **Frequency of headache medication used (doses/month):** 6.5 (4.6) **Intensity of pain (median, IQR):** 39 (26-55) **MSQoL (median, IQR):** 58 (51-67)	physiotherapist. Between sessions they practised at home every day with a CD. Adherence was defined as participating in 6 or more sessions at the clinic. Verbal confirmation of practice at home was also required. **All groups** 4- 12 week baseline period, followed by 12 week treatment period. All participants were allowed to contract the physiotherapist or neurologist with questions (telephone or visit). No restriction was made on the use of concomitant acute medication.			

Abbreviations: NR=not reported, M/F=male/female, N= number of patients, SD=Standard deviation, SE=Standard error, ITT=Intention to treat analysis, CI=confidence interval, MSQoL=Migraine specific quality of life, ICHD=International Classification of Headache Disorders