

## Neurowetenschappelijk onderzoek gericht op werkingsmechanismen

Onderstaand volgt een lijst met relevante literatuur op alfabetische volgorde van de achternaam van de auteur. De lijst is samengesteld door M.M. Klaver, voormalig neuroloog en SOLK-deskundige. De artikelen zijn voorzien van een korte annotatie (in groen) en gerangschikt in enkele rubrieken:

- Pijn
- Pijn-Emotie
- Emotievorming
- Emotieregulatie
- Emotie-persoonlijk geheugen
- Neuroanatomie van de emotie
- Stress

### PIJN

Bingel U, Schoell E, Herken W, Büchel C, May A. Habituation to painful stimulation involves the antinociceptive system. *Pain* 2007;131(1-2):21-30.

The decreased perception of pain over time is related to increased responses in the subgenual anterior cingulate cortex (sgACC) over time.

**Het genugebied sgACC remt en habitueert pijn.**

Mazzola L, Isnard J, Peyron R, Mauguière F. Stimulation of the human cortex and the experience of pain: Wilder Penfield's observations revisited. *Brain*. 2012;135:631-40.

The medial parietal operculum and posterior insula are thus the only areas where electrical stimulation is able to trigger activation of the pain cortical network and thus the experience of somatic pain.

**Pijngewaarwording vindt plaats in de insula, niet in de hersenschors.**

Staud R, Craggs JG, Robinson ME, Perlstein WM, Price DD. Brain activity related to temporal summation of C-fiber evoked pain. *Pain*. 2007;129(1-2):130-42.

Neural responses related to temporal summation are evoked in somatosensory processing areas (THAL, S2), and other pain functions such as cognition (ACC, PFC), affect (INS, ACC, PAG), pre-motor activity (SMA, cerebellum), and pain modulation (rostral ACC).

**C-vezel activiteit is nauw verbonden met sensitisatie.**

Taylor KS, Seminowicz DA, Davis KD. Two systems of resting state connectivity between the insula and cingulate cortex. *Hum Brain Mapp*. 2009 ;30(9):2731-45.

A resting state anterior insula-pACC/aMCC cingulate system that may integrate interoceptive information with emotional salience to form a subjective representation of the body, involving in environmental monitoring, response selection, and skeletomotor body orientation.

**Insula (input) en gyrus cinguli (output) bedienen lichaamsgevoel en bewegen in de ruimte.**

Wiech K, Kalisch R, Weiskopf N et al. Anterolateral prefrontal cortex mediates the analgesic effect of expected and perceived control over pain. *J Neurosci*. 2006;26(44):11501-9.

Self-controlled stimulation was accompanied by less pain and anxiety and higher activation in dorsal anterior cingulate, right dorsolateral, and bilateral anterolateral prefrontal cortices. Externally controlled pain, activation in right anterolateral was inversely correlated with the participants' general belief to have control over their lives.

**Zelfcontrole en externe locus of control reguleren de pijn via verschillende routes.**

Xie YF, Huo FQ, Tang JS. Cerebral cortex modulation of pain. *Acta Pharmacol Sin*. 2009;30(1):31-41.

Contrary to the traditional view that the cerebral cortex is not involved in pain perception. The pain processing network includes the anterior cingulate cortex, the insular cortex, the primary and secondary somatosensory cortices, the ventrolateral orbital cortex and the motor cortex. These cortical structures constitute the medial and lateral pain systems.

**Twee pijnsystemen bedienen acute en chronische pijn.**

Yang L, Symonds LL. Neural substrate for facilitation of pain processing during sadness. *Neuroreport*. 2012 Oct 24;23(15):911-5.

The 'emotional-processing' regions included the subgenual cingulate cortex and the amygdala. We suggest that increased activation in the posterior insula/SII is part of a top-down system of pain facilitation that includes the anterior cingulate cortex, amygdala, and periaqueductal gray.

**Het genugebied kan pijn versterken/sensitiseren en dempen/habitueren.**

## **PIJN-EMOTIE**

Baliki MN, Chialvo DR, Geha PY, et al. Chronic pain and the emotional brain: specific brain activity associated with spontaneous fluctuations of intensity of chronic back pain. *J Neurosci*. 2006 ;26(47):12165-73.

Subjective spontaneous pain of CBP involves specific spatiotemporal neuronal mechanisms, distinct from those observed for acute experimental pain, implicating a salient role for emotional brain concerning the self.

**Het zelf is betrokken bij chronische pijn.**

Burns JW, Holly A, Quartana P et al. Trait Anger Management Style Moderates Effects of Actual ("State") Anger Regulation on Symptom-Specific Reactivity and Recovery Among Chronic Low Back Pain Patients. *Psychosom Med*. 2008; 70(8): 898–905.

Results implicate lower paraspinal muscle tension as a potential physiological mechanism that links the actual inhibition of anger following provocation to chronic pain severity among chronic low back pain patients.

**Ingehouden boosheid verhoogt meetbaar de spierspanning in de lage rug.**

Eisenberger NI, Lieberman MD, Williams KD. Does rejection hurts? An fMRI study of social exclusion. *Science* 2003;302:209-92.

Paralleling results from physical pain studies, the anterior cingulate cortex (ACC) was more active during exclusion than during inclusion and correlated positively with self-reported distress.

**Sociale pijn/uitsluiting/afwijzing maakt gebruik van het mediale pijnsysteem.**

Hashmi JA, Baliki MN, Huang L, Baria AT, Torbey S, Hermann KM, Schnitzer TJ, Apkarian AV. Shape shifting pain: chronification of back pain shifts brain representation from nociceptive to emotional circuits. *Brain* 2013 Sep;136(Pt 9):2751-68.

The results demonstrate that brain representation for a constant percept, back pain, can undergo large-scale shifts in brain activity with the transition to chronic pain.

**Bij chronisch worden van de pijn verplaatst de activiteit van het acute/nociceptieve systeem naar het chronische emotieve pijnsysteem.**

Masten CL Eisenberger NI, Borofsky LA, et al. Neural correlates of social exclusion during adolescence: understanding the distress of peer rejection. *Soc Cogn Affect Neurosci.* 2009;4(2):143-57.

Findings unique to adolescents indicated that activity in the subgenual anterior cingulate cortex (subACC) related to greater distress, and that activity in the ventral striatum related to less distress and appeared to play a role in regulating activity in the subACC and other regions involved in emotional distress.

**Bij pubers is het genugebied actief bij afwijzingspijn.**

Richter M, Eck J, Straube T, Miltner WH, Weiss T. Do words hurt? Brain activation during the processing of pain-related words. *Pain* 2010;148:198-205.

However, when attention was focused on a foreground task and words were presented in the background (distraction task), we found a decrease in activation within dorsal anterior cingulum and a relative increase in activation within the subgenual ventral anterior cingulum (sACC) when processing pain related words compared to other words.

**Woorden op de achtergrond net als 'onbewuste'woorden activeren het genugebied.**

## **EMOTIEVORMING**

Butler T, Pan H, Epstein J et al. Fear-related activity in subgenual anterior cingulate differs between men and women. *Neuroreport* 2005;16(11):1233-6.

The subgenual anterior cingulate cortex is a region critical for emotional control with a greater susceptibility of women to anxiety and affective disorders.

**Vrouwen zijn limbisch in het genugebied actiever dan mannen bij emotievorming.**

Etkin A, Egner T, Kalisch R. Emotional processing in anterior cingulate and medial prefrontal cortex. *Trends Cogn Sci.* 2011;15(2):85-93.

Dorsal-caudal regions of the ACC and mPFC are involved in appraisal and expression of negative emotion, whereas ventral-rostral portions of the ACC and mPFC have a regulatory role with respect to limbic regions involved in generating emotional responses.

**Emotieregulatie vindt plaats in het dorsale/cognitieve systeem (bewust relativeren) en het ventrale/emotieve systeem (flink zijn).**

Haas BW, Omura K, Constable RT, Canli T. Emotional conflict and neuroticism : personality-dependent activation in the amygdala and subgenual anterior cingulate. *Behav neurosci.* 2007;121(2):249-56.

Neuroticism correlated positively with amygdala and subgenual AC activation during trials of high emotional conflict, compared with trials of low emotional conflict.

**Het genugebied is betrokken bij een emotioneel conflict.**

Kanaan RA, Craig TK, Wessely SC, David AS. Imaging repressed memories in motor conversion disorder. *Psychosom Med.* 2007;69(2):202-5.

Cued recall of the clinically repressed event was associated with emotional arousal, including the amygdala and right inferior frontal lobe activations. Such recall was also associated with decreased motor activity in the area corresponding to the subjectively paralyzed limb.

**De onbewuste stressor (cued recall) zorgde voor veranderde limbische activiteit en niet de vermeende bewuste emotie.**

Mayberg HS, Liotti M, Brannan SK, McGinnis S, et al. Reciprocal limbic-cortical function and negative mood: converging PET findings in depression and normal sadness. *Am J Psychiatry.* 1999 May;156(5):675-82.

With sadness reciprocal changes involving subgenual cingulate and right prefrontal cortex occur with both transient and chronic changes in negative mood.

**Het genugebied is actief bij de vorming en expressie van verdriet.**

Nili U, Goldberg H, Weizman A, Dudai Y. Fear thou not: activity of frontal and temporal circuits in moments of real-life courage. *Neuron* 2010;66(6):949-62.

Activity in the sgACC was positively correlated with the level of fear upon choosing to overcome fear but not upon succumbing to it. The amygdala, was attenuated as the level of fear increased when choosing to overcome fear.

**Genugebied en amygdala remmen elkaar over en weer afh. van de context. Bij moed domineert het genugebied, bij overgave de amygdala.**

Rubio A, Van Oudenhove L, Pellissier S, et al. Uncertainty in anticipation of uncomfortable rectal distension is modulated by the autonomic nervous system--a fMRI study in healthy volunteers. *Neuroimage* 2015;107:10-22.

Uncertain anticipation of rectal distension involved several relevant brain regions, namely activation of sgACC and medial prefrontal cortex and deactivation of amygdala and insula.

**Bij onzekerheid is het limbisch systeem actief.**

Ramirez-Mahaluf JP, Perramon J, Otal B, et al. Subgenual Anterior Cingulate Cortex Controls Sadness-Induced Modulations of Cognitive and Emotional Network Hubs. *Sci Rep*, 2018;8(1):8566.

These hub areas (DL and mPFC) did not modulate their mutual functional connectivity following sadness but they did so through an interposed area, the subgenual anterior cingulate cortex (sACC).

**Het genugebied bemiddelt bij de prefrontale connectiviteit en bestuurt zo context en perspectief.**

Zahn R, Moll J, Paiva M, et al. The neural basis of human social values: evidence from functional MRI. *Cereb Cortex.* 2009 Feb;19(2):276-83.

During self-agency, activity in the anterior ventromedial prefrontal cortex correlated with pride and guilt, whereas activity in the subgenual cingulate solely correlated with guilt.

**Het genugebied is betrokken bij het schuldgevoel.**

## EMOTIEREGULATIE

Banks SJ, Eddy KT, Angstadt M, Nathan PJ, Phan KL. Amygdala-frontal connectivity during emotion regulation. *Soc Cogn Affect Neurosci*. 2007 ;2(4):303-12.

We show that activity in specific areas of the frontal cortex (dorsolateral, dorsal medial, anterior cingulate, orbital) covaries with amygdala activity and that this functional connectivity is dependent on the reappraisal task.

**Verschillende prefrontale en cingulaire gebieden beïnvloeden de amygdala activiteit.**

Campbell-Sills L, Simmons AN, Lovero KL et al. Functioning of neural systems supporting emotion regulation in anxiety-prone individuals. *Neuroimage* 2011 ;54(1):689-96.

Compared to healthy controls, anxious participants showed greater activation of brain regions implicated in effortful (lateral PFC) and automatic (subgenual anterior cingulate cortex) control of emotions during down-regulation of negative emotions.

**Angst vraagt meer bewuste prefrontale en onbewuste automatische activiteit bij remming van de negatieve emotie/amygdala activiteit dan bij controles.**

Lieberman MD, Eisenberger NI, Crockett MJ, et al. Putting feelings into words: affect labeling disrupts amygdala activity in response to affective stimuli. *Psychol Sci*. 2007;18(5):421-8.

Ventrolaterale PFC and amygdala activity during affect labeling were inversely correlated, a relationship that was mediated by activity in medial prefrontal cortex (mPFC). These results suggest that affect labeling may diminish emotional reactivity along a pathway from ventrolateral to mPFC to the amygdala.

**Benoemen remt amygdala activiteit.**

Ochsner KN, Gross JJ. The cognitive control of emotion. *Trends Cogn Sci*. 2005 May;9(5):242-9. Review.

Controlling attention to, and cognitively changing the meaning of, emotionally evocative stimuli, these two forms of emotion regulation depend upon interactions between prefrontal and cingulate control systems and cortical and subcortical emotion-generative systems.

**Aandacht en verandering van perspectief reguleren langs verschillende routes de limbische emotievorming.**

Ochsner KN, Ray RR, Hughes B, et al. Bottom-up and top-down processes in emotion generation: common and distinct neural mechanisms. *Psychol Sci*. 2009 Nov;20(11):1322-31.

Both types of responses activated the amygdala, although bottom-up responses did so more strongly. Self-reported affect correlated with activity in the amygdala during bottom-up responding and with activity in the medial prefrontal cortex during top-down responding.

**Emotieproces: beïnvloeding emotievorming en emotieregulatie over en weer. Primaire amygdala activiteit is sterker dan secundaire prefrontale regulatie. Zelfregulatie speelt zich mediaal prefrontaal af.**

Silvers JA, McRae K, Gabrieli JD, et al. Age-related differences in emotional reactivity, regulation, and rejection sensitivity in adolescence. *Emotion*. 2012 Dec;12(6):1235-47.

Adolescents' emotional lives are attributable to developmental changes in emotional reactivity or emotion regulation. Age effects on regulation success was unrelated to emotional reactivity. Young adolescents with high in rejection sensitivity were less successful at regulating responses to social than to nonsocial stimuli.

**Emotieregulatie neemt toe met de leeftijd, maar de emotionele reactiviteit blijft dezelfde. Pubers met een sterke afwijzingsgevoeligheid hebben meer moeite met emotieregulatie.**

Williams LM, Liddell BJ, Kemp AH, Bryant RA, Meares RA, Peduto AS, Gordon E. Amygdala-prefrontal dissociation of subliminal and supraliminal fear. *Hum Brain Mapp*. 2006;27(8):652-61.

Cortically, subliminal fear was distinguished by right ventral anterior cingulate activity and supraliminal fear by dorsal anterior cingulate and medial prefrontal activity. Although subcortical amygdala activity was relatively persistent for subliminal fear, supraliminal fear showed more sustained cortical activity.

**Onbewuste processen schakelen bewuste corticale activiteit niet in en houden de activiteit binnen het subcorticale/limbische domein.**

## **EMOTIE-PERSOONLIJK GEHEUGEN**

Bonnici HM, Chadwick MJ, Lutti A, Hassabis D, Weiskopf N, Maguire EA. Detecting representations of recent and remote autobiographical memories in vmPFC and hippocampus. *J Neurosci*. 2012;32(47):16982-91.

vmPFC contained information about recent and remote autobiographical memories, although remote memories were more readily detected there, indicating that consolidation or a change of some kind had occurred.

**vmPFC speelt een rol bij oude herinneringen.**

Kross E, Davidson M, Weber J, Ochsner K. Coping with emotions past: the neural bases of regulating affect associated with negative autobiographical memories. *Biol Psychiatry* 2009;65(5):361-66.

Activity in a network of regions involved in self-referential processing and emotion, including subgenual anterior cingulate cortex and medial prefrontal cortex, was highest in response to the feel strategy and lowest for the accept strategy.

**Persoonlijke emoties tonen de meeste activiteit in het genugebied en vmPFC bij voelen/betrokkenheid en minder bij zakelijk accepteren.**

Gillihan SJ, Xia C, Padon AA, Heberlein AS, Farah MJ, Fellows LK. Contrasting roles for lateral and ventromedial prefrontal cortex in transient and dispositional affective experience. *Soc Cogn Affect Neurosci*. 2011;6(1):128-37.

These findings suggest a role for VM in modulating *dispositional* negative affect; in contrast, VL areas appear to be critical in regulating *transient* emotional responses while emotional stimuli are present.

**vmPFC is actief bij oud zeer (dispositionele emoties) en vlPFC is actief bij tijdelijke actuele emoties.**

## NEUROANATOMIE VAN DE EMOTIE

Kim Y, Sakata H, Nejime M, et al. Afferent connections of the dorsal, perigenual, and subgenual anterior cingulate cortices of the monkey: Amygdalar inputs and intrinsic connections. *Neurosci Lett*. 2018 Aug 10;681:93-99.

sgACC and pgACC exhibit opposite emotion-related activity patterns and that an interaction of the ACC with the amygdala is crucial for emotion-related ACC functions. pgACC directly influences the activity of the sgACC .  
**In het genugebied beïnvloeden pgACC en sgACC elkaar, afh. van context en amygdala activiteit.**

Palomero-Gallagher N, Eickhoff SB, Hoffstaedter F, et al. Functional organization of human subgenual cortical areas: Relationship between architectonical segregation and connectional heterogeneity. *Neuroimage*. 2015 Jul 15;115:177-90.

sACC areas presented distinct co-activation patterns within widespread networks encompassing cortical and subcortical regions. They shared common functional domains related to emotion, perception and cognition.

**Het genugebied is het knooppunt voor emotievorming met lichamelijke, sociale en cognitieve invloeden.**

Phillips ML, Drevets WC, Rauch SL, Lane R. Neurobiology of emotion perception I: The neural basis of normal emotion perception. *Biol Psychiatry* 2003;54:504-14.

Studies indicate two neural systems: *a ventral system*, including the amygdala, insula, ventral striatum, and ventral regions of the anterior cingulate gyrus and prefrontal cortex, predominantly important for automatic regulation of emotional responses; and *a dorsal system*, including the hippocampus and dorsal regions of anterior cingulate gyrus and prefrontal cortex, predominantly important for the regulation of the affective state.

**Er zijn twee prefrontale systemen: een dorsaal/cognitief systeem en een ventraal/emotief systeem.**

Quirk GJ, Likhtik E, Pelletier JG, Paré D. Stimulation of medial prefrontal cortex decreases the responsiveness of central amygdala output neurons. *J Neurosci*. 2003 Sep 24;23(25):8800-7.

mPFC gates impulse transmission from the basolateral to central, perhaps through GABAergic intercalated cells, thereby gating the expression of conditioned fear.

**De amygdala heeft een poortmechanisme vmPFC activiteit door te laten of te blokkeren.**

Sakata H, Kim Y, Nejime M, et al. Laminar Pattern of Projections Indicates the Hierarchical Organization of the Anterior Cingulate-Temporal Lobe Emotion System. *Front Neuroanat*. 2019 Jul 31;13:74.

sgACC crucial for emotional responses based on sensory and mnemonic inputs from the anterior temporal lobe, whereas the pgACC is more related to the cognitive control of emotion.

**In het genugebied is pgACC betrokken bij cognitieve invloed en sgACC bij emotieve prikkels en vroegere ervaring.**

Wager TD, Davidson ML, Hughes BL, et al. Prefrontal-subcortical pathways mediating successful emotion regulation. *Neuron*. 2008;59(6):1037-50.

Two separable pathways: (1) a path through nucleus accumbens that predicted greater reappraisal success, and (2) a path through ventral amygdala that predicted reduced reappraisal success (i.e., more negative emotion).

**Onder het ventrale systeem ligt het primaire systeem met een beloningsroute naar de accumbens en een strafroute naar de amygdala.**

## **STRESS**

Brosschot JF, Verkuil B, Thayer JF. Conscious and unconscious perseverative cognition: is a large part of prolonged physiological activity due to unconscious stress? *J Psychosom Res*. 2010;69(4):407-16.

Our recent studies have shown that increased activity of the autonomic nervous system continues after conscious perseverative cognition has stopped: It goes on for several hours and even during sleep. This and several other findings suggest that a considerable part of increased physiological activity may be due to unconscious perseverative cognition.

**Onbewust piekeren houdt de verhoogde autonome activiteit/stress in stand.**

Dum RP, Levinthal DJ, Strick PL. Motor, Cognitive, and Affective Areas of the Cerebral Cortex Influence the Adrenal Medulla. *Proc Natl Acad Sci*. 2016;113(35):9922-7.

Two broad networks have access to the adrenal medulla. A major component of this network originates from the supplementary motor area and the cingulate motor areas. These cortical areas are involved in all aspects of skeletomotor control. The second, smaller network originates in the pregenual and subgenual regions of anterior cingulate cortex.

**Twee centrale routes beïnvloeden de bijnier: de ene vanuit het supplementaire motore gebied en de ander vanuit het genugebied.**

Tawakol A, Ishai A, Takx RA, et al. Relation between resting amygdalar activity and cardiovascular events: a longitudinal and cohort study. *Lancet*. 2017 Feb 25;389(10071):834-845.

Amygdalar activity independently and robustly predicted cardiovascular disease events. Amygdalar activity is involved partly via a path that includes increased bone-marrow activity and arterial inflammation. These findings provide novel insights into the mechanism through which emotional stressors can lead to cardiovascular disease in human beings.

**Amygdala activiteit is sterk verbonden met cardiovasculaire gebeurtenissen.**

Wang J, Rao H, Wetmore GS et al. Perfusion functional MRI reveals cerebral blood flow pattern under psychological stress. *Proc Natl Acad Sci U S A*. 2005 ;102(49):17804-9.

Psychological stress induces negative emotion and vigilance and that the ventral PFC right plays a key role in the central stress response.

**Het ventrale systeem speelt een belangrijke rol bij stress.**