COGNITIVE DYSFUNCTION IN CHRONIC PAIN.

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NORSK SMERTEFORENING (NOSF)
The Norwegian Pain Society
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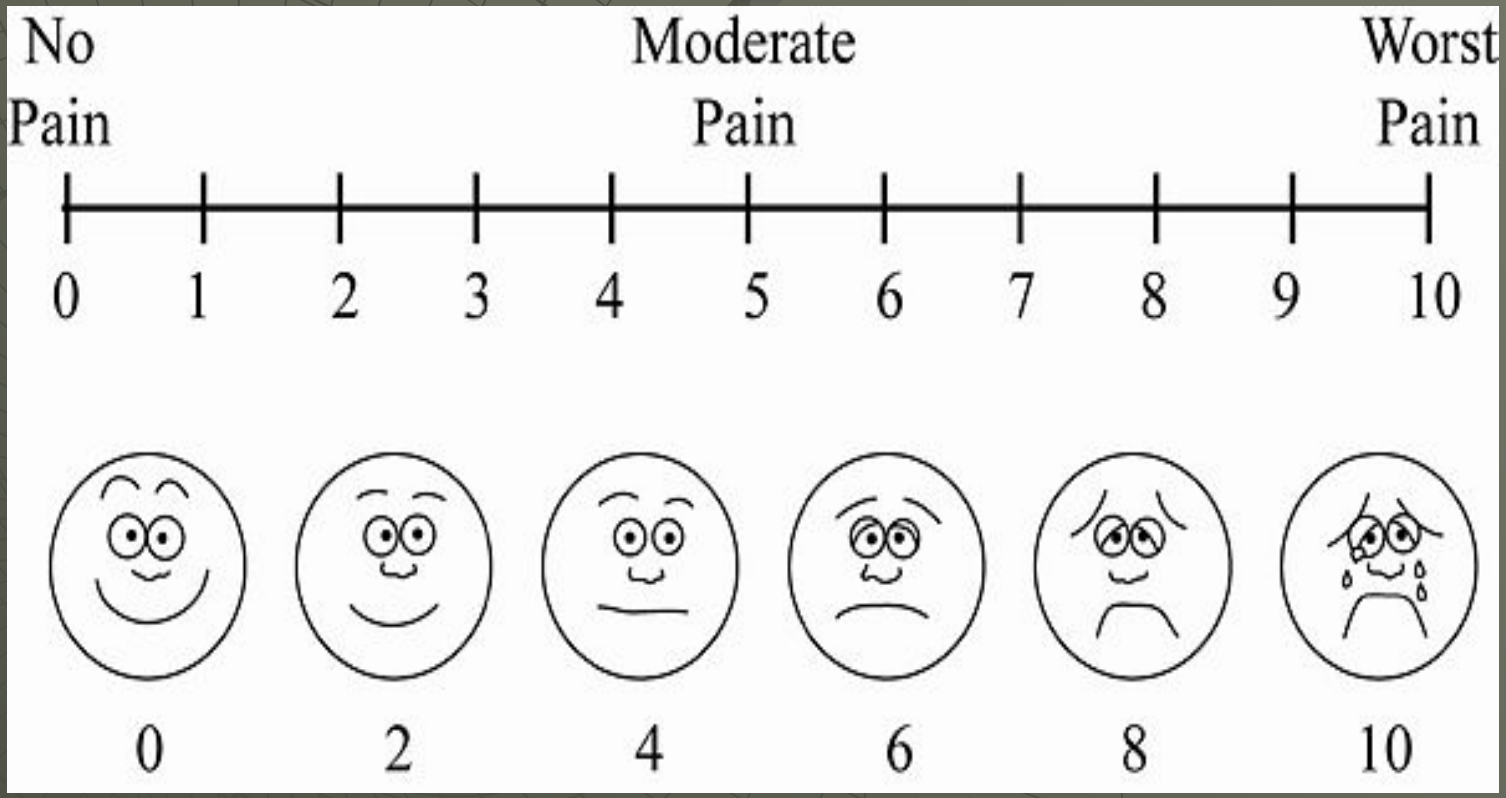
CHRONIC(any pain lasting more than 12 weeks)NON-MALIGNANT PAIN

CHRONIC PAIN. AVERAGE PAIN INTENSITY OF 4 OR MORE OVER AT LEAST 12 WEEKS.



OVERVIEW (IMPORTANT ISSUES)

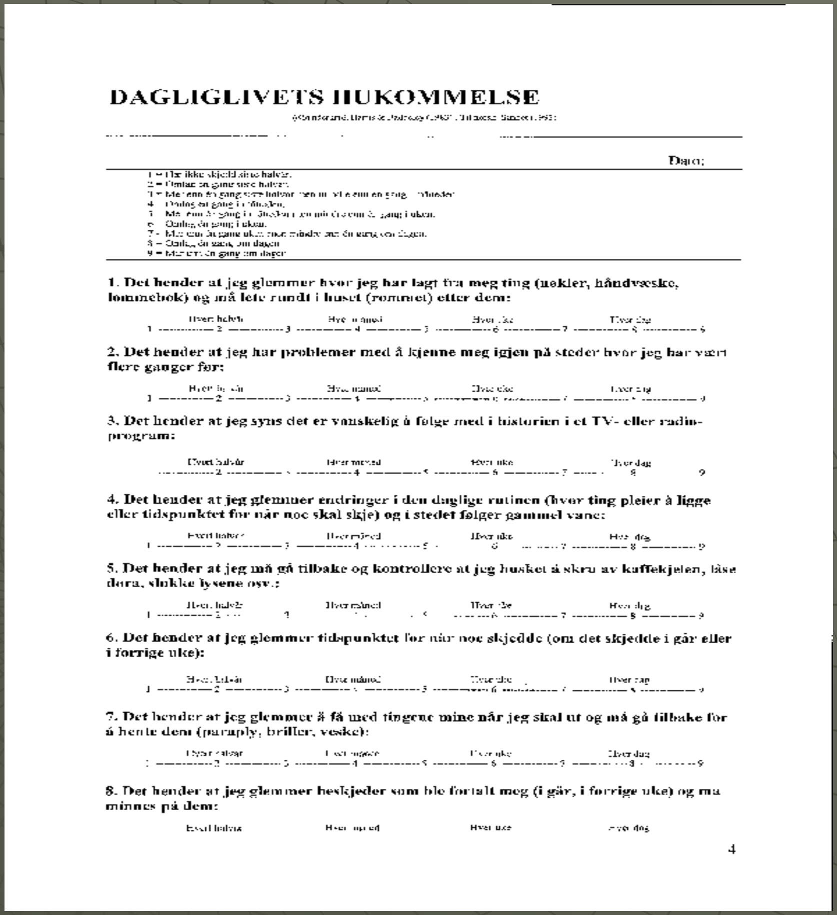
- From subjective complaints to objective dysfunction.
- What kinds of cognitive impairments are due to chronic pain and how are they operationalized/assessed ?
- Possible effects of use of opioids on neuropsychological functioning in chronic pain.
- Causal mechanisms (”pain demands attention” AND possible brain mechanisms of pain perception and regulation).

SUBJECTIVE COMPLAINTS OF COGNITIVE/NEURPSYCHOLOGICAL IMPAIRMENTS

-
- Patients with chronic pain frequently complain of cognitive impairments that causes difficulties in social situations and everyday functioning.

- Such subjective complaints my reflect genuine impaired function, or, alternatively, represent the patients' self perception although no objective dysfunction exists.

EVERYDAY MEMORY QUESTIONANIRE (EMQ).



DAGLIGLIVETS HUKOMMELSE

Dato:

1 = Har ikke skjedd siste halvår.
2 = Omtrent én gang siste halvår.
3 = Mer enn én gang siste halvår, men mindre enn én gang i måneden.
4 = Omtrent én gang i måneden.
5 = Mer enn én gang i måneden, men mindre enn én gang i uken.
6 = Omtrent én gang i uken.
7 = Mer enn én gang i uken, men mindre enn én gang om dagen.
8 = Omtrent én gang om dagen.
9 = Mer enn én gang om dagen.

1. Det hender at jeg glemmer hvor jeg har lagt fra meg ting (nøkler, håndveske, lommebok) og må lete rundt i huset (rommet) etter dem:

Hvert halvår — Hver måned — Hver uke — Hver dag
1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9

2. Det hender at jeg har problemer med å kjenne meg igjen på steder hvor jeg har vært flere ganger før:

Hvert halvår — Hver måned — Hver uke — Hver dag
1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9

3. Det hender at jeg syns det er vanskelig å følge med i historien i et TV- eller radio-program:

Hvert halvår — Hver måned — Hver uke — Hver dag
1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9

4. Det hender at jeg glemmer endringer i den daglige rutinen (hvor ting pleier å ligge eller tidspunktet for når noe skal skje) og i stedet følger gammel vane:

Hvert halvår — Hver måned — Hver uke — Hver dag
1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9

5. Det hender at jeg må gå tilbake og kontrollere at jeg husket å skru av kaffekjelen, låse døra, slukke lysene osv.:

Hvert halvår — Hver måned — Hver uke — Hver dag
1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9

6. Det hender at jeg glemmer tidspunktet for når noe skjedde (om det skjedde i går eller i forrige uke):

Hvert halvår — Hver måned — Hver uke — Hver dag
1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9

7. Det hender at jeg glemmer å få med tingene mine når jeg skal ut og må gå tilbake for å hente dem (paraply, briller, veske):

Hvert halvår — Hver måned — Hver uke — Hver dag
1 — 2 — 3 — 4 — 5 — 6 — 7 — 8 — 9

8. Det hender at jeg glemmer beskjeder som ble fortalt meg (i går, i forrige uke) og må minnes på dem:

Hvert halvår — Hver måned — Hver uke — Hver dag

4

COGNITIVE / NEUROPSYCHOLOGICAL CONSEQUENCES OF CHRONIC PAIN (not with brain involvement).

- A number of controlled studies indicate that chronic pain is associated with cognitive/neuropsychological impairments/changes.
- The most common changes are in the areas of attention, psychomotor speed and working memory.
- Executive functions/Decision making and memory can also be impaired.
- OBS: It is well known that even mild/moderate cognitive changes have detrimental effects on psychosocial function and quality of life.

- **Hart et al. (2000). Chronic pain and neuropsychological functioning. *Neuropsychology Review*, 10; 131-149.**
- **Moriarty et al. (2011) The effect of pain on cognitive function: a review of clinical and preclinical research. *Progress in Neurobiology*, 93, 385-404.**
- **Berryman et al. (2013). Evidence for working memory deficits in chronic pain: A systematic review and meta-anlysis. *Pain*, 154, 1181-1196.**

COGNITVE IMPAIRMENTS ASSOCIATED WITH CHRONIC PAIN.

- The majority of previous studies are hampered by typically assessing selected types of patients, like for example fibromyalgia, whip lash, low back pain or headache. An exception is Sjøgren et al. (2005) ; included a heterogenuous sample chronic non-malignant pain patients treated in a multidisciplinary pain centre.

- NB: A limitation with this study is that it did not include a reasonable range of cognitive/neuropsychological tasks covering the main functional areas (Continuous Reaction Time, Finger Tapping, PASAT).

- Sjøgren et al. (2005). Neuropsychological assessment of chronic non-malignant pain patients treated in a multidisciplinary pain centre. *European Journal of Pain*, 9, 453-62.

Landrø, Fors, Våpenstad, Holthe, Stiles & Borchgrevink (2013).
The extent of neurocognitive dysfunction in a multidisciplinary pain centre population. Is there a relation between reported and tested neuropsychological functioning? *Pain,* 154, 972-977

- The main research questions of the current study were:
- (1) Is there a relation between self-reported and performance-based neuropsychological functioning in patients referred to a multidisciplinary pain centre when controlling for depressive symptoms?
- (2) To what extent are main objective neuropsychological functions impaired in a pain clinic population and does neuropsychological functioning vary across subgroups (localized vs generalized vs neuropathic pain)?
- (3) Do pain medications reduce neuropsychological functions in chronic pain patients?

Landrø, Fors, Våpenstad, Holthe, Stiles & Borchgrevink (2013).
The extent of neurocognitive dysfunction in a multidisciplinary pain centre population. Is there a relation between reported and tested neuropsychological functioning? *Pain,* 154, 972-977

- 72 chronic pain patients consecutively recruited in a multidisciplinary pain centre (St. Olav Hospital/NTNU).
- Divided into 3 subcategories:
- Generalized pain (for example fibromyalgia) (n=28)
- Localized pain(like low back and neck pain) (n=30)
- Neuropathic pain (i.e. pain arising as a direct consequence of a lesion or disease affecting the somatosensory system).
- (n=14).

Landrø, Fors, Våpenstad, Holthe, Stiles & Borchgrevink (2013).
The extent of neurocognitive dysfunction in a multidisciplinary pain centre population. Is there a relation between reported and tested neuropsychological functioning? *Pain,* 154, 972-977

- **No between sub group differences**:
- Age
- Pain (Brief Pain Inventory, mean last weak)
- Depressive symptoms (Beck Depression Inventory)
- Cognitive Complaints (Everyday Memory Questionnaire; EMQ).
- General IQ (Vocabulary and Matrices from WAIS-III).

Landrø, Fors, Våpenstad, Holthe, Stiles & Borchgrevink (2013).
The extent of neurocognitive dysfunction in a multidisciplinary pain centre population. Is there a relation between reported and tested neuropsychological **functioning? *Pain,* 154, 972-977**

Cognitive variables	EMQ	Depression	EMQ controlled for depression
Stroop test I	-.31 *	-.23	-.21
Stroop test II	-.29 *	-.20	-.20
Stroop test III	-.33 **	-.29 *	-.25 *
Stroop test IV	-.33 **	-.22	-.29 *
CVLT Learning	-.28 *	-.23	-.09
WAIS L-N	-.10	-.08	-.03
PASAT	-.02	-.12	.06

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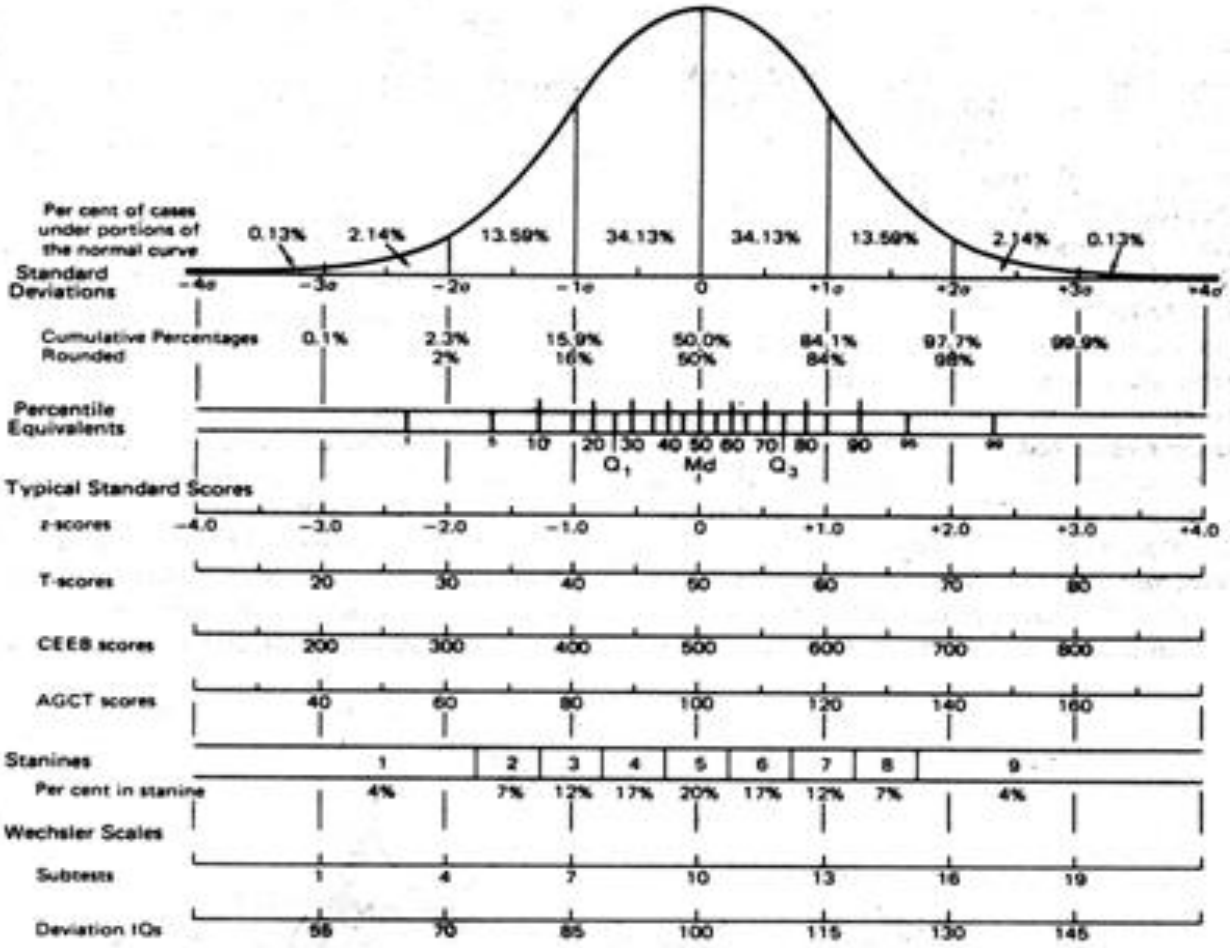
THE NORMAL DISTRIBUTION CURVE.



Landrø, Fors, Våpenstad, Holthe, Stiles & Borchgrevink (2013).
The extent of neurocognitive dysfunction in a multidisciplinary pain centre population. Is there a relation between reported and tested neuropsychological **functioning?** ***Pain,*** **154, 972-977**

Neuropsychological variables	Total pain (n = 72)	Generalized pain (n = 28)	Localized pain (n = 30)	Neuropathic pain (n = 14)
	< 1.5 SD (< 2.0 SD)	< 1.5 SD (< 2.0 SD)	< 1.5 SD (< 2.0 SD)	< 1.5 SD (< 2.0 SD)
CVLT learning	11% (4.1%)	10.7% (7.1%)	6.7% (0%)	21.4% (7.1%)
WAIS L-N sequencing	20.5% (5.5%)	25.0% (7.1%)	16.7% (3.3%)	21.4% (7.1%)
PASAT	17.6% (8.8% [c] *)	22.2% (11.1%)	7.4% (0%)	23.1% (15.4%)
Stroop test I	20.8% (11.1% [c] ***)	35.7% (25.0%)	10.3% [a] * (0% [a] ***)	14.3% (7.1%)
Stroop test II	17.8% (9.6%)	21.4% (7.1%)	16.7% (10%)	14.3% (7.1%)
Stroop test III	18.1%[c] ** (11.1%)	28.6% (14.3%)	3.4% [a] *** (3.4%)	28.6% [b] * (21.4%)
Stroop test IV	18.1% (9.7%)	28.6% (14.3%)	6.9% [a] * (3.4%)	21.4% (14.3%)

Landrø, Fors, Våpenstad, Holthe, Stiles & Borchgrevink (2013).
The extent of neurocognitive dysfunction in a multidisciplinary pain centre population. Is there a relation between reported and tested neuropsychological functioning? *Pain,* 154, 972-977.

- Cognitive complaints in chronic pain patients are significantly associated with objective test performance in the area of inhibitory control after partialling out degree of depressive symptoms.
- A larger proportion of patients with generalized and neuropathic pain performed below clinically significant cut-off, whereas patients with localized pain exhibited impaired function to a lesser degree.
- Chronic pain patients receiving opioids did not perform worse than patients off opioid treatment.

Opioids:Neuropsychological consequences.

- RELATIVELY FEW DIFFERENCES HAVE BEEN FOUND WHEN COGNITIVE PERFORMANCE IN CHRONIC PAIN PATIENTS IS COMPARED WITH THEIR PERFORMANCE BEFORE TAKING OPIOIDS, OR WITH THE PERFORMANCE OF A COMPARABLE PAIN POPULATION NOT TAKING OPIOIDS.

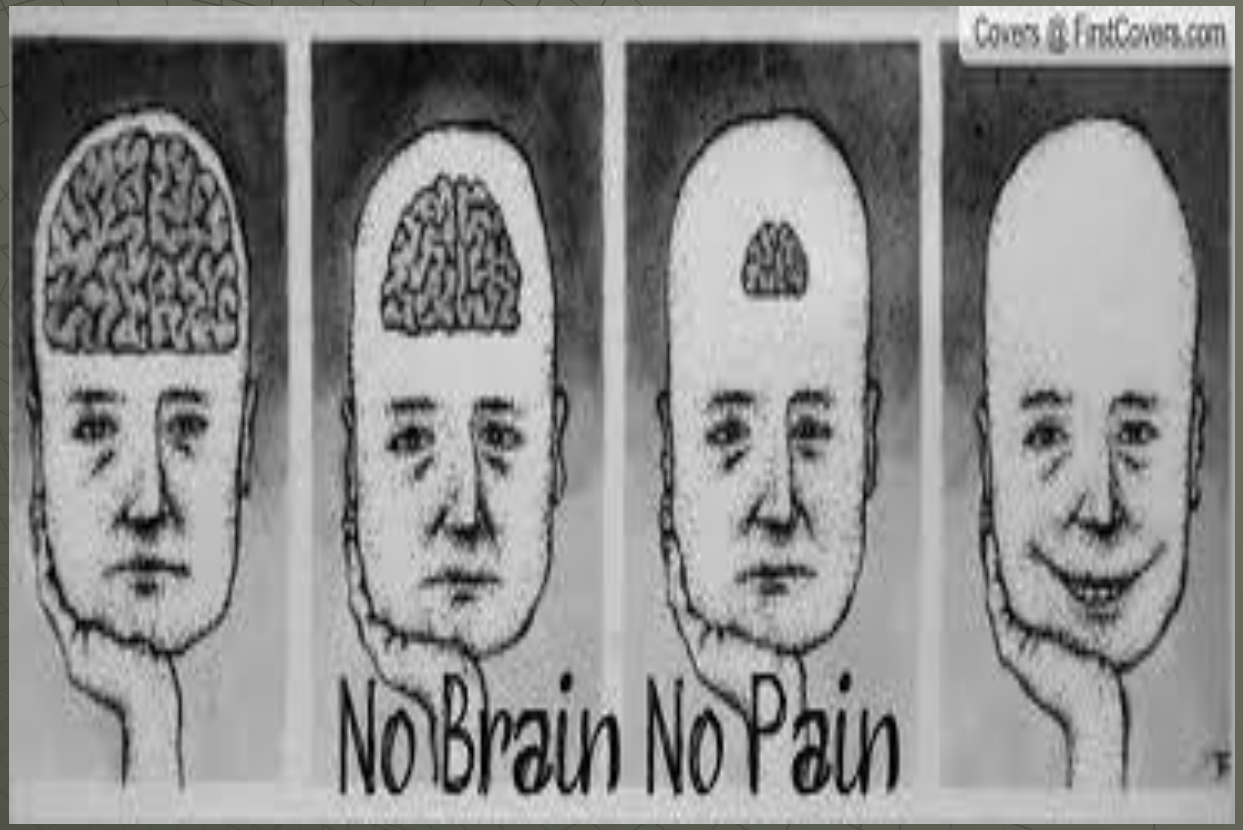
- Chapman et al. (2002). Effects of intermediate- and long-term use of opioids on cognition in patients with chronic pain. *The Clinical Journal of Pain*, 18, S83-S90.

Opioids:Neuropsychological consequences

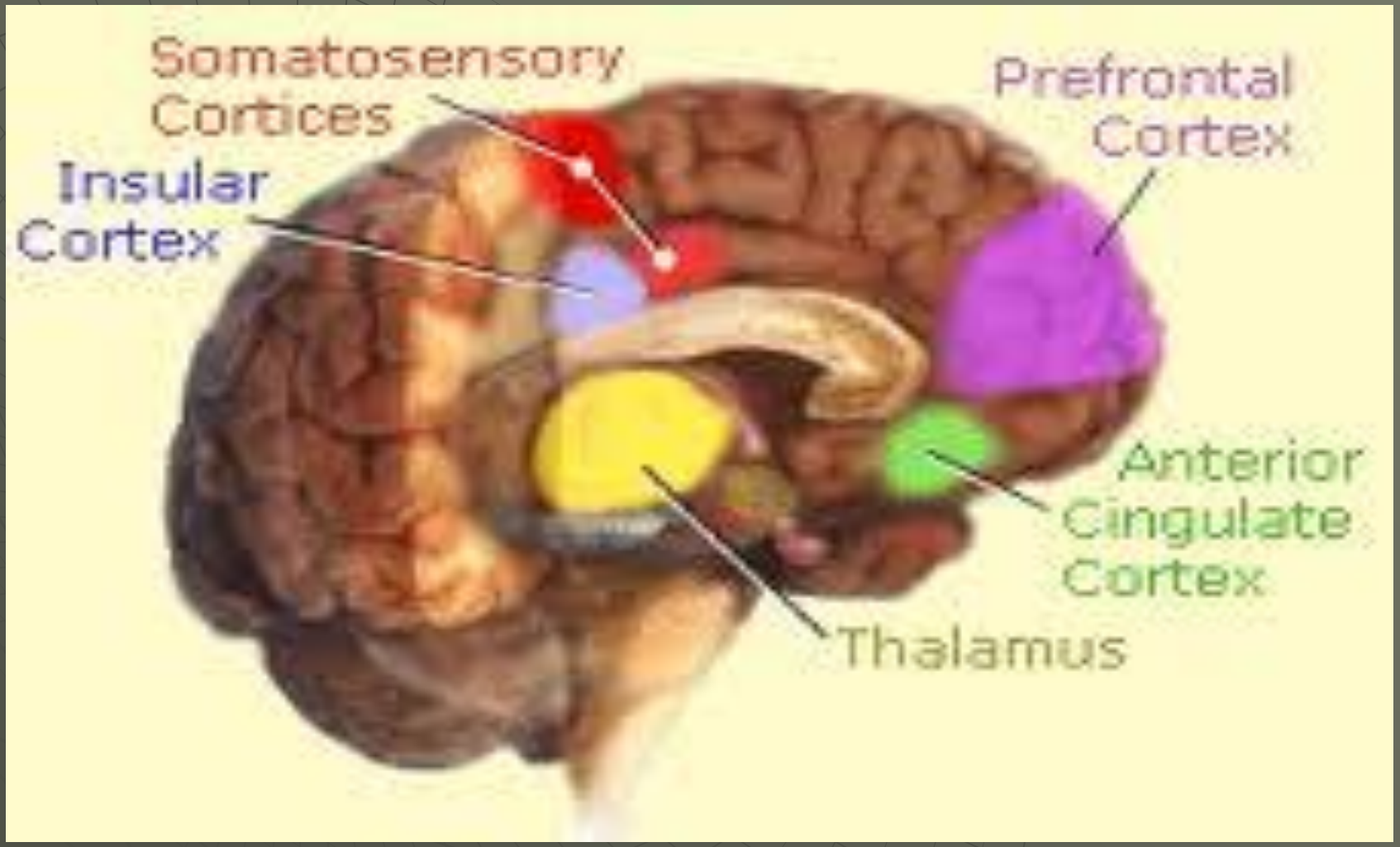
- «…this review differs from previous reviews by excluding non-controlled and experimental studies, opioid treatment for less than a week, and by quality rating studies. On the basis of this high quality evidence pertaining to long-term opioid treatment and cognition, current evidence for benefit, harm or lack of appreciable effect of long-term stable opioid treatment on cognitive functioning in non-cancer patients is still limited».

- Kendall et al. (2010). The cognitive effects of opioids in chronic non-cancer pain. *Pain*, 150 (2), 225-230

Although the brain itself can not feel pain (no pain receptors)……



A unique cerebral signature for pain.



Chronic pain and cognitive/neuropsychological changes. Possible causal mechanisms.

- ”Pain demands attention”).
- The anterior cingulate cortex is involved in both pain processing and in basic allocation of cognitive resources.
- Thus, cognitive capacity can be limited due to chronic pain.
- Chronic pain could be redefined as chronic interruption.
- Eccleston & Crombez (1999). Pain demands attention- a cognitive-affective model of the interruptive function of pain. *Psychological Bulletin*, 125, 356-66.

Chronic Back Pain Is Associated with Decreased Prefrontal and Thalamic Gray Matter Density

Apkarian et al. (2004). *Journal of Neuroscience,* 24, 10410-15.

Abstract

The role of the brain in chronic pain conditions remains speculative. We compared brain morphology of 26 chronic back pain (CBP) patients to matched control subjects, using magnetic resonance imaging brain scan data and automated analysis techniques. CBP patients were divided into neuropathic, exhibiting pain because of sciatic nerve damage, and non-neuropathic groups. Pain-related characteristics were correlated to morphometric measures. Neocortical gray matter volume was compared after skull normalization. Patients with CBP showed 5-11% less neocortical gray matter volume than control subjects. The magnitude of this decrease is equivalent to the gray matter volume lost in 10-20 years of normal aging. The decreased volume was related to pain duration, indicating a 1.3 cm3 loss of gray matter for every year of chronic pain. Regional gray matter density in 17 CBP patients was compared with matched controls using voxel-based morphometry and nonparametric statistics. Gray matter density was reduced in bilateral dorsolateral prefrontal cortex and right thalamus and was strongly related to pain characteristics in a pattern distinct for neuropathic and non-neuropathic CBP. Our results imply that CBP is accompanied by brain atrophy and suggest that the pathophysiology of chronic pain includes thalamocortical processes.

Chronic pain shrinks people's brains.

- The results don't reveal why the brain shrinks, but it might involve degradation of neurons, which are the signal transmitters of the mind and body.
- "It is possible it's just the stress of having to live with the conditions", Apkarian told *Life Science.* The neurons become overactive or tired of the activity.
- Another posibility is that people born with smaller numbers of neurons are predisposed to suffering chronic pain. But some of the differences "must be directly related to the condition", Apkarian said.

PERSPECTIVE: Oosterman et al. (2010). A unique association between cognitive inhibition and pain sensitivity in healthy subjects. *European Journal of Pain,* 14, 1046-1050.

En (v)ond sirkel ??

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Landrø, Fors, Våpenstad, Holthe, Stiles & Borchgrevink (2013). Response to letter to the Editor. *Pain*, 155, 643-647

- ***To the Editor:***
- **Reneman et al. [5] challenge our article [3] and the accompanying editorial commentary by McGuire [4] concluding that the evidence for pain-related cognitive impairment is growing. They state, "It has been well established that in this patient group performance validity on neuropsychological tests is poor: 25% to 75% of patients with chronic pain fail on performance or symptom validity tests." They document this "well-established" fact with only a single reference [2]. Further, it only addresses complex regional pain syndrome I patients. Finally and most importantly, they conceal that in this study, "all were incentivized by a disability-seeking context" (cited from the abstract), and "All but one participant were referred by either an insurer or attorney" (cited from the Methods section). Reneman et al. should be aware that their statements could be perceived to mistrust a whole group of patients with chronic pain to be potentially simulants.**
- **In our study, we tested 72 patients who were consecutively examined in our multidisciplinary pain center. They were referred by their doctors for treatment for their severe pain, not by an insurance company or an attorney for a disability evaluation. They were informed that their participation in the research project would not affect the treatment they were about to receive. So what would be their motive to actively underperform in the research setting?**
- **…… In our research project, the forced-choice subtask of the California Verbal Learning Test II (CVLT-II), which is often used as a performance validity test, was also administered. None of our participants performed below the expected level, but as a result of the reasoning above, we thought it would be redundant to report the results from this CVLT-II subtask.**
- **…….Another comment in the letter of Reneman et al. is that we should have investigated the relationship between test scores and daily life activities. We agree that this is an important issue, but this is a peculiar objection to our study because this was not one of our main research questions.**
- **We fully agree that pain syndromes are complex, implicating interrelations among biological, psychological, and social factors. However, we are convinced that scientific progress within this field must build on clearly defined research questions and operationalizations, not vague and nonbinding statements like "everything is related to everything."**

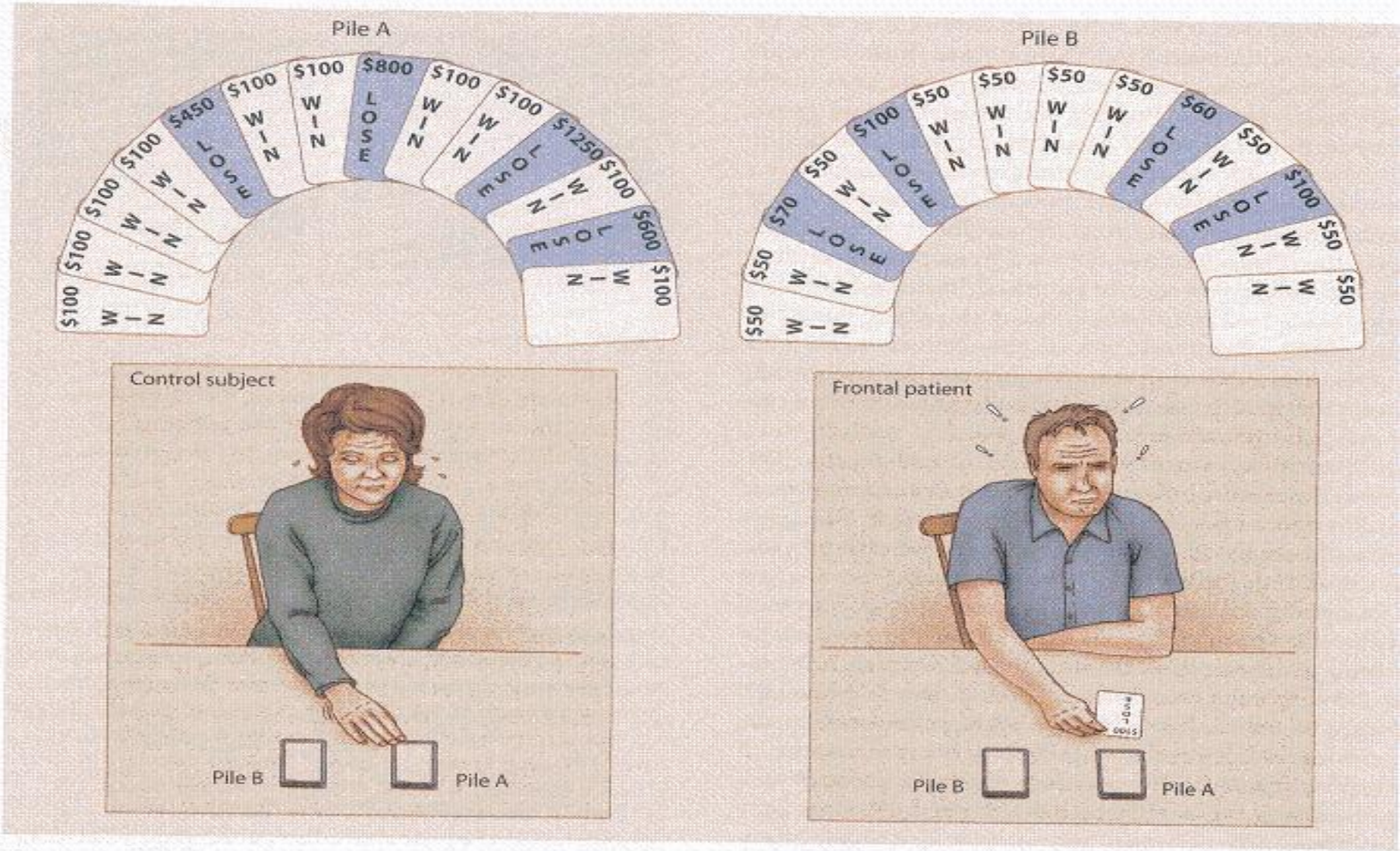


Figure 11.25 Emotional responses occur in reaction to stimuli, but also are useful in guiding our decision processes. Subjects were required to choose cards from one pile or the other, with each card specifying an amount won or lost. Through trial and error, the subjects could learn that pile A was riskier than pile B. Control subjects not only tended to avoid the high-risk pile, but also showed a large GSR when considering choosing a card from this pile. The patients with prefrontal lesions failed to show these anticipatory GSRs. Interestingly, they did show a large GSR upon turning over a card and discovering they had lost $1000 (of play money).

- Abstract
- Patients with chronic pain have impaired cognitive functions, including decision making, as shown with the Iowa gambling task (IGT). The main aim of this study was to elucidate whether patients' decision making is associated with a lack of the anticipatory skin conductance response (SCR). An increase in anticipatory SCR before making unfavorable choices is known to guide decisions in healthy controls during the IGT. Since several brain regions involved in decision making are reported to have altered morphology in patients with chronic pain, the second aim was to explore the associations between IGT performance and brain structure volumes. Eighteen patients with chronic pain of mixed etiology and 19 healthy controls matched in terms of age, sex, and education were investigated with a computerized IGT during the recording of SCR, heart rate, and blood pressure. The participants also underwent neuropsychological testing, and three-dimensional T1-weighted cerebral magnetic resonance images were obtained. Contrary to controls, patients did not generate anticipatory SCRs before making unfavorable choices, and they switched between decks of cards during the late phase of the IGT significantly more often, and this was still observed after adjusting for depression scores. None of the other autonomic measures differed during IGT performance in either group or between groups. In patients, IGT scores correlated positively with total cortical grey matter volume. In controls, there was no such association, but their IGT scores correlated with the anticipatory SCR. It may be speculated that the reduction in anticipatory SCRs makes the chronic pain patients rely more on cortical resources during decision making.
- KEYWORDS:
- Iowa gambling task; autonomic measures; cortex; magnetic resonance imaging; skin conductance response

- Elvemo, N., Nilsen, K.B., Landrø, N.I., Borchgrevink, P.C. & Håberg, A.K. (2014). Patients with chronic pain lack somatic markers during decision-making. *Journal of Pain Research*, 7, 425-327.

Other topics.

- Standard short battery for the clinic !
- Can it be reversed…..Cog Med project.

WORKING MEMORY

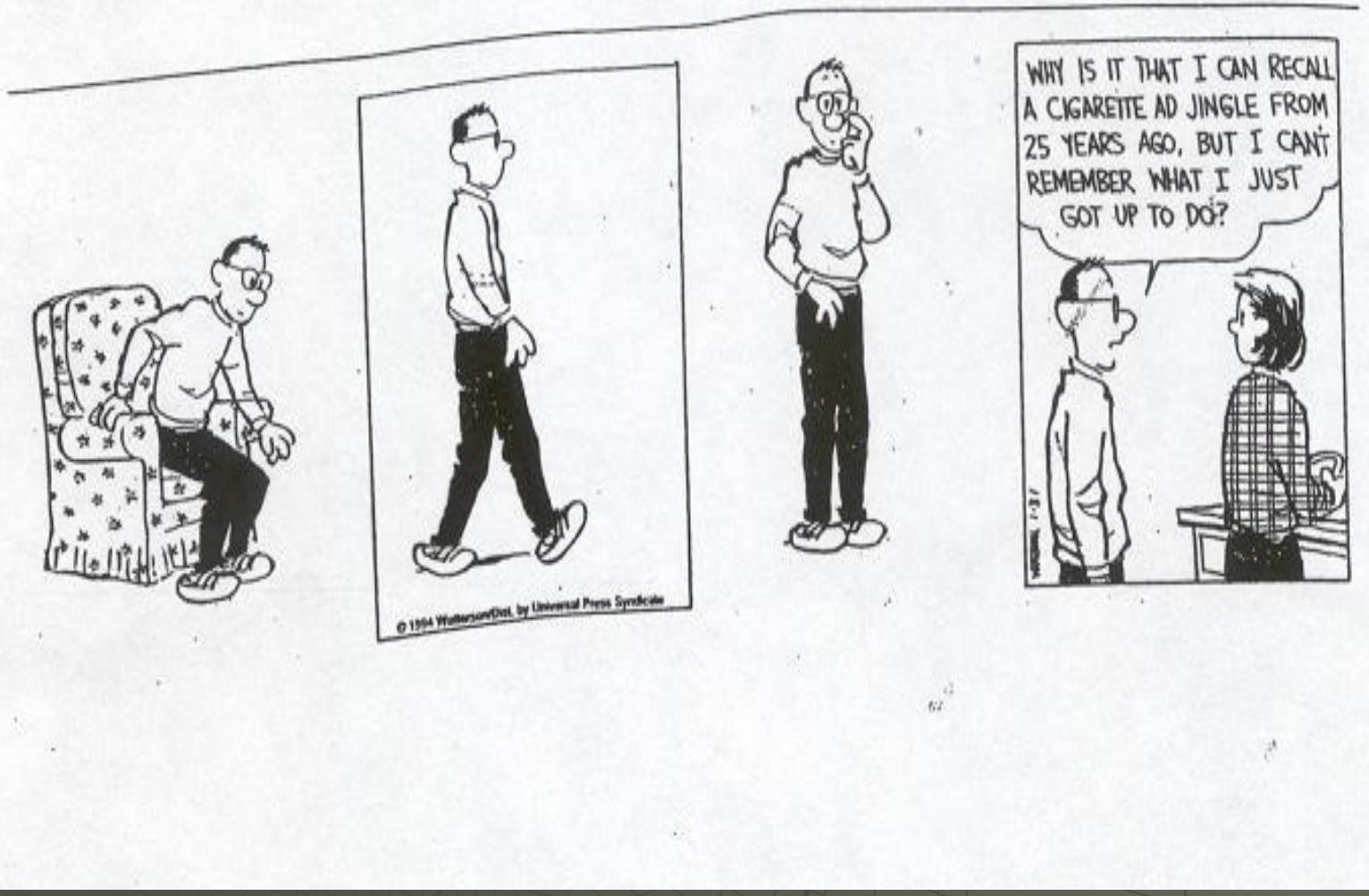
TO PROCESS INFORMATION EFFECTIVELY,

THE BRAIN NEEDS A SYSTEM TO HOLD

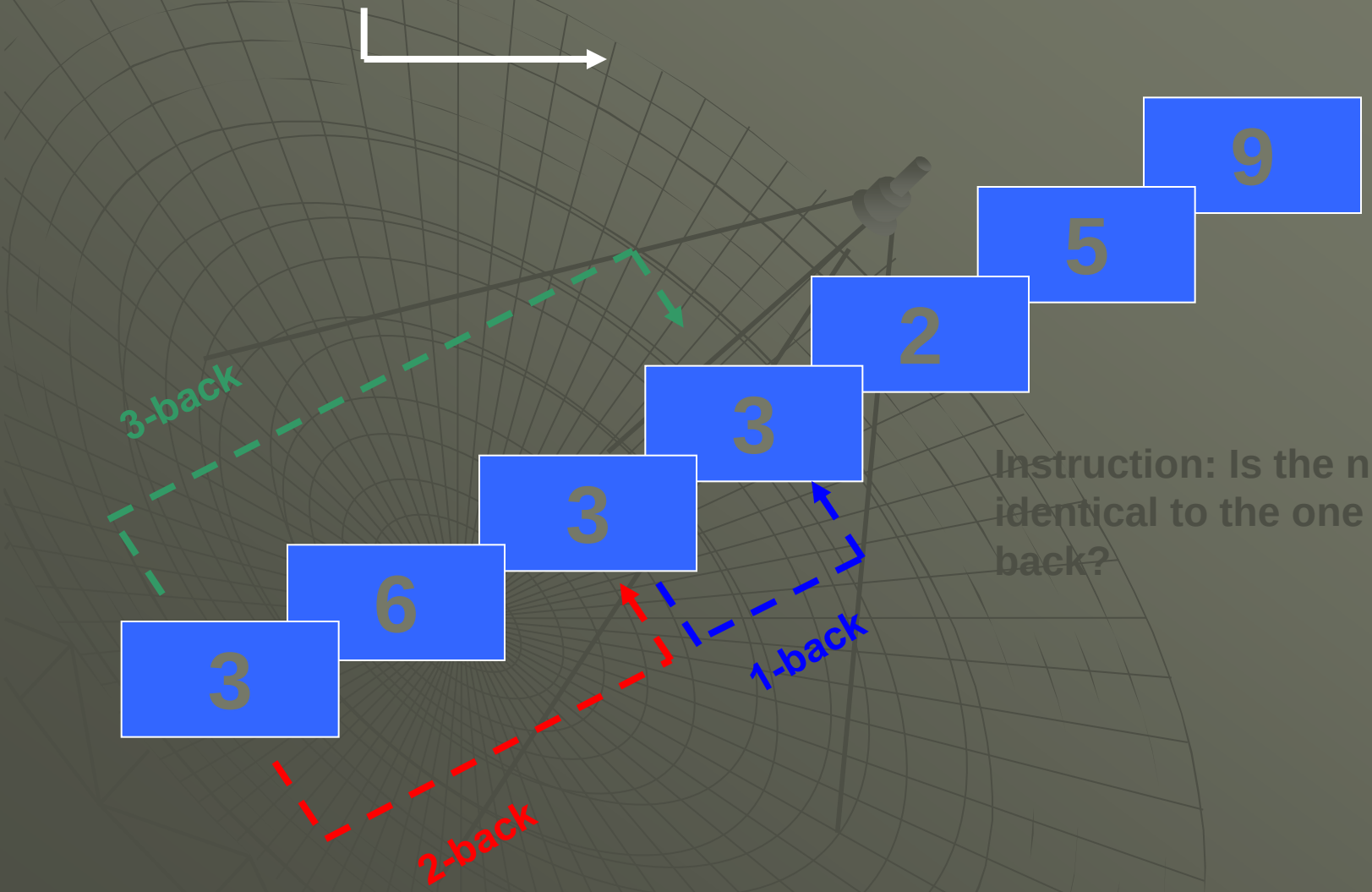
INFORMATION BRIEFLY ON-LINE:

THE BLACKBOARD OF THE MIND.

”PERHAPS THE MOST SIGNIFICANT ACHIEVEMENT OF HUMAN MENTAL EVOLUTION” (GOLDMAN-RAKIC, 1992, WORKING MEMORY AND THE MIND, *SCIENTIFIC AMERICAN*, *267*, 110-117.)


WHY IS IT THAT I CAN RECALL A CIGARETTE AD JINGLE FROM 25 YEARS AGO, BUT I CAN'T REMEMBER WHAT I JUST GOT UP TO DO?
© 1994 WattersonDist. by Universal Press Syndicate

- n-back task



Instruction: Is the number identical to the one n places back?

”PSYKOLOGISK” SMERTE OG HJERNEN

Smerte+hjerte=sant

Forsøk viser at knuste hjerter gjør like vondt som knuste ribbein.

Tekst: **Linda Lund Nilssen**
lnn@aftenbladet.no

Vi har lenge visst hva som skjer i hjernen ved fysisk skade. «Smertesenteret», anterior cingulate cortex aktiviseres, og sender signaler om ... ja, smerte, beordrer reparasjon, og så videre. Psykolog Matthew Lieberman og Naomi Eisenberger ved universitetet i California, og Kipling Williams ved Macquarie-universitetet i Sydney bestemte seg for scanne reaksjonen i hjernen ved følelsesmessig smerte, melder The Guardian.

Og fant at følelsesmessig smerte er mye sterkere fortundet med fysisk smerte enn vi har vært klar over.

Forsøkene ble utført med videospill

1 Kaste ball

Forsøkspersonen ble fortalt at hun skulle kaste ball med to andre mennesker i et videospill. Men menneskene eksisterte ikke, hele spillet ble styrt av datamaskinen.

Magnettomografi

Forsøkspersonens hånd

2 Ekskluderes

Etter en stund tar de datamaskinkontrollerte spillerne over. De kaster bare ballen til hverandre. Forsøkspersonen ekskluderes – får ikke lenger delta i spillet.

3 «Smertesenter»
(Anterior cingulate cortex)

Forskerne registrerer all aktivitet i hjernen under spillet med magnettomografi.
Følelsen av å være ekskludert ga store utslag i hjerneaktiviteten – i det samme senter som aktiviseres ved fysisk smerte.

KILDE: Science