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# Aspects of causality

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# Aspects of Causality: A Verdict inquiry of a Case with SSRI Use

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Abstract: Sometimes more than one expert advises the court. They use different notional frameworks in doing so, and may report different opinions about the case they examined. In this case, the authors discuss the relation between the use of a serotonin reuptake inhibitor (SSRI) and a fatal tragedy in a family where the mother was accused of killing her husband and daughter a few days after use of the SSRI. No fewer than seven experts were heard (four behavioral experts, one behavioral toxicologist, one pharmacist and one pharmacologist) at the ensuing trial, and various possible diagnoses were dealt with in the experts' reports and at trial. More attention must be paid to the mentally debilitating influence of SSRI medication on certain psychological functions shortly after its intake. Although a mono-causal relationship between that influence and the accused's intention is necessary to exculpate the accused from guilt, the authors believe that a singular connection is never happened the case.

Keywords: Violence, medication, causality, judgment.

#### 1. Introduction

The effects of a drug on behavior can be disastrous, but as presumed, in only very rare cases is there a causal relation between the drug in question and a violent act, fortunately.

As more scientists participate in criminal trials, greater clarity about the circumstances or the cause of a violent offence does not automatically result. Amongst other things, this has to do with the interpretation of the facts by various disciplines, each with their own professional thought patterns, methods and testing procedures. For the court to be able to get an overall impression, it must at least be aware of the methods of the various expert witnesses and actors (such as the public prosecutor, the accused, behavioral experts and medical specialists) in order to meaningfully integrate the evidence and arrive at a legal conclusion or verdict. Here, a case was discussed

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which several experts were heard in a court proceeding, who each reported to the court from their own notional framework, and from which the court had to arrive at a verdict in relation to the facts and opinions offered.

Oei [1] stated the notional frameworks that the various parties use during the trial are different. In his opinion, the legal, the behavioral and the judicial relationship frameworks were applied. Starting with the judicial framework, the following issues are relevant: offence, possible disorder and danger of re-offending and possible treatment. Note that the accused often (erroneously) thinks that there is no disorder whatsoever. In those cases, however, it is possible to discuss the desired treatment with the accused. Also, the accused scores positive points with the court if he shows willingness for treatment. In this way the accused hopes to escape an unconditional prison sentence or court order, and instead, 'to get off' with a suspended sentence with an added condition of

being treated by an institution or expert appointed by the court. Furthermore, if the accused does not have a disorder, the court cannot attribute the possible danger or re-offending to one. For, without a disorder there can be no unaccountability and no exemption of culpability.

The lawyer has a slightly different perspective from the accused, as follows: possible offence, possible disorder, danger of re-offending if there is a disorder, accountability, and meting out of punishment. Also, the alleged facts of the offence must first be legally proven, assuming they give rise to a punishable offence.

Next, the behavioral expert's framework takes into account the following considerations: possible disorder, then the relationship with the possible offence, determination of accountability, possible danger of re-offending as a result of the disorder, and possibilities for treatment.

In determining an accused's accountability, the following questions must be answered from the behavioralist's perspective: is there a pathological disorder at the time the punishable offence was committed? If yes, is the causal relationship between the disorder and the punishable offence adequately plausible? Again, if yes, how should accountability be assessed in the light of the first two questions and all circumstances of the case? The presence of a disorder contributes to recidivism in the behavioral expert's point of view; however, the question of recidivism is only asked if the question about a relevant disorder has been answered in the affirmative.

Before Oei's work, Brouwers, Drost and Oei [2] had already concentrated on the question of whether medication can have undesired effects, or may even give rise to violent behavior. As far as the authors know there is no drug that always causes violence in everyone who takes it. Moreover, some people are always prone to violent behavior when they take a certain drug, as is the case for instance with alcohol.

Furthermore, some drugs sometimes produce a temporary change in the psychological condition of some people. If during that period something happens—a threat, or a provocation, for example—the person can respond with violence. Still, one needs a possible victim to commit a violent crime.

To elaborate upon the last point, consider the following. A serotonin reuptake inhibitor (SSRI) can produce a temporary state of depersonalization. If, during that period a man is unexpectedly and suddenly dismissed from his employment, he may become so angry that he wants to kill his boss. Normally he will not do that, but then, in this state of depersonalization he goes to the house of his boss and is ready to shoot him. The boss is not at home and while the man is on his way back the depersonalized state disappears and he asks himself, "What am I doing?" It is realistic to say that probably in most of the cases there no violent act during the temporarily changed condition because there was no opportunity, or no possible victim. But there can be a causal relation if both circumstances exist. By taking the medication a temporary disorder may occur, causing the person to behave differently than usual, but without that particular drug there is no disorder or no offence, nor any danger of re-offending. In the end the violent behavior is the result of chance. If for instance ten thousand people use that drug, perhaps a thousand of them will temporarily experience depersonalization, a hundred of them will experience a serious life event during depersonalization, and ten of them will want to react with violent behavior towards that event, five will have a possible victim available as well, and finally, one will produce a victim. Different levels of damage will result in the one instance, depending on how the victim responded to the threat.

In relation to a real case, which concerns a well-considered, instrumental form of violence, the question arose whether a drug, in particular, an anti-depressant (an SSRI) can cause a temporary mental disorder leading to a violent offence.

## 2. Methods

To illustrate the different processes as illustrated in an actual case report, a search was done in the Netherlands' verdict register. This register is freely accessible to the public. Because it is essential to go step-by-step in time to ascertain if the perpetrator knew, or could have known, what the consequences were of taking this kind of medicine the following search criteria were used: use of an SSRI during violent act, start of SSRI use no longer than four weeks (prior to the violent act), the verdict must contain enough facts and multidisciplinary contributions, and the violent act having occurred as recently as possible to complement discussions of other, past cases. Applying these criteria, four cases were found, but only one case provided sufficient facts to formulate the within analysis.

Also, in order to determine if there is any reason to believe that there could be a relationship between (recent) use of SSRI and violence the literature on this topic was reviewed and summarized.

#### 3. Results

## 3.1 Description of the case

The woman had been suffering from bouts of depression since 1996, for which she was treated with medication each time. Specifically, since 2003, she had been prescribed the drug paroxetine (an SSRI). She also suffered a sub-arachnoid haemorrhage, the exact location of which was never determined. In June 2008 she was in a seriously depressed state once more, and on 6 August of that year, she was prescribed paroxetine again, 20 milligrams once daily. The woman did not fill this prescription. When she consulted the physician she had discussed whether she needed psychological aid. Her daughter very much wished the woman would accept this kind of assistance. She had promised her daughter she would agree to this kind of treatment, but only after discussing it with her own GP, which was the reason why she had not yet taken the prescribed drug. On 3 September 2008, she consulted her own GP, and as in the meantime there had been no improvements in her depressive complaints, the prescribed dose of paroxetine was augmented to 20 mg twice daily. Arriving home, she started at once with three tablets of paroxetine and also two tablets of oxazepam, for unknown reasons. The following day she took two more pills of paroxetine, but no more oxazepam.

The night of 4 and 5 September, after midnight, the woman met her daughter at Schiphol Airport, Amsterdam. Her daughter asked the woman about her discussions with the GP and the woman said that she had chosen the drug and not the psychological assistance, unlike her earlier promise to her daughter. The daughter got very cross with her mother. This conflict created a bad atmosphere in the home, and after her husband and her daughter had gone off to bed, the woman was very shaken and sad.

She sat on her settee and experienced an overwhelming feeling that she did not want to live any more. At the same time she felt that she could not cause the grief that her suicide would inflict upon her husband and daughter, and so she decided to take them with her in death. She then made fairly extensive preparations of her farewell and subsequently went looking in the home for a means by which to kill them. She found an axe in the garage. The woman struck her husband in the head several times with the axe, and then thought, "Two more to go", meaning herself and her daughter. After having killed her daughter with the axe as well, she tried to commit suicide by running her car into a tree. She had by then already called the emergency number (at 4.59 a.m.) and announced that she had committed murder. The woman was wounded in the collision with the tree and was taken to hospital. At 9.05 a.m. (5 September), blood samples were taken, which were later analyzed by the NFI (Dutch Forensic Institute). In the blood, traces (< 10 ng/mL whole blood) of paroxetine were found.

There are plenty of questions concerning this case, for instance: what is the function of paroxetine in the violent acts? Is it a dominant, monocausal, or contributory (facilitating) function? Is the contribution of paroxetine dose-dependent? How quickly do changes occur? Can a temporary mental disorder be caused by it? Are there differences in result where the violence is impulsive or instrumental?

#### 3.2 SSRIs and violence

By open discussions of cases, such as the one just described, attention is drawn to important, hitherto unknown side effects of drugs [3]. Whether there is indeed a causal relationship between the use of the drug and the phenomenon observed cannot be directly deduced from this, however. That said, scientifically proving causality is not essential: rather, identifying the possibility for suicide and violence brings about attentiveness after the drug in question has been prescribed. Only very rarely do the opinions of the various experts contrast. Such contrasts, however, do occur in the question of whether anti-depressants in general, and SSRIs in particular, may give rise to suicide and violence. Reports highlight an additional, complicating factor, that is, that especially children and young people are susceptible [4-6].

Healy, Herxheimer and Menkes [7] described a possible relationship between SSRIs and violence. In addition, SSRI stories [8] listed over two hundred cases in which a relation between murder, suicide and an anti-depressant was suggested. Lareb [9] identified that, until June 2009, 24 cases were reported to the Dutch Side Effects Centre in which the use of an SSRI and aggression coincide (8 cases of Paroxetine, 5 cases of Citalopram, 4 cases of Fluoxetine, 4 cases of Fluvoxamine, 2 cases of Escitalopram and 1 case of Sertraline). They suggested a possible relation between **SSRIs** and aggression. Europe Eudravigilance [10] reported 700 serious cases and WHO data also supported the association. Special attention should be given to this association, considering the nature of the adverse drug reaction and the possible consequences. Thus, the relationship between SSRIs and violence (suicide, homicide) cannot be excluded.

In spite of these reports the chance of violence (suicide, homicide) being brought about by the use of anti-depressants must be considered to be extremely small [11-14]. But this does not necessarily mean that this relationship is negligibly small in individual cases. And there is understandable issue as to whether the risk is "not demonstrable" and "non-existent".

It has not been proved that the use of an SSRI may give rise to an aggressive incident, but it is plausible. This is in line with knowledge gained by general experience, that is, that the use of psychoactive substances (the best known example is alcohol) may give rise to incidents of aggression. SSRIs are psychoactive substances and they affect the nature and the intensity of emotional processes (e.g. anger). Thus, it is possible that under certain circumstances SSRIs contribute to the occurrence of an aggressive incident. By this the authors mean that the use of the medication plays an important part in the occurrence of the incident under prevailing conditions and at that particular moment. Without the use of the drug, the occurrence of the phenomenon, e.g. aggression, outburst of anger, outburst of violence, emotions running amuck etc. would have been considerably less likely. What is the mechanism that triggers the aggression?

The initial idea was that aggression was the result of disinhibiting suicidal impulses: a depressive disorder goes together with suicidal desires and plans, but also with inhibitions, which stop the suicide from taking place. By treatment with anti depressants the activity, energy level of the patient improve, before improving his mood. Because inhibitions disappear, some people commit suicide during the first phase of the treatment. The biochemical explanatory model pointed to the consequences of various kinds of neurotransmission (adrenerg and serotonerg). The

adrenerg effect was thought to be especially important for the impulse (drive) and the serotonerg for the mood. Later this is turned out to be too simple for a rendition of the facts. The serotonerg system plays a part in mood, that is, fear as well as aggression. Even a distinct serotonin-dependent subtype of depression has been postulated, in which aggression is the first symptom [15]. In other words, SSRIs appear not just to influence mood. Also, SSRIs cause mental deregulations, such as a withdrawal symptoms, during the initial phase of treatment or after the treatment has been stopped. Quite soon after starting treatment in some people, an increase of fear phenomena like increased jitteriness, impulse outbursts, fear of dying occur. Such symptoms may also occur after a sudden end of the treatment. People might become aggressive as a result of this feature of treatment with SSRIs.

A second possible explanation for the occurrence of (auto) aggression after the start of the treatment with SSRIs are side effects such as akathisia, which is the urge to move about and feelings of unrest, unwellness, inner unrest, or depersonalization. There are various ideas about the method through which akathisia triggers aggression. Loonen and Stahl describe a biological mechanism in which akathisia is basically an artificial form of being motivated to get moving [16]. The patient is uncontrollably provoked into executing certain (aggressive) behavior. Another idea is that akathisia constitutes a torment to such an extent that people in their desperation become (auto) aggressive. This side effect is typical anti-psychotic medications, but is a regular feature of SSRIs [17-19], for instance, with fluoxetine showing an incidence rate of between 10% and 25%. Akathisia is also a symptom of a serotonerg syndrome featuring mental phenomena such as restricted awareness, (auto) aggression, neuromuscular phenomena and autonomous instability.

In an attempt to illuminate the mechanism of SSRI-induced aggression, two forms of animal aggression are relevant: defense and hunt (or, assertive) aggression [20]. Of these two forms of aggression there is an example in rodents where administering anti-depressants had the opposite effect, namely, the inhibition of defensive aggression and the promotion of assertive aggression [21]. It is postulated that in order to initiate these two forms there is in principle an emotional, affective or "hot" form of aggression as well as a cognitive, instrumental or "cold" one. The emotionally initiated form shows strong resemblance to the fear reaction and is triggered by the amygdala, or the almond core of the brain, where the emotional component (anger) is primarily triggered. On the other hand, the cognitively which initiated form of aggression results from a careful analysis of the circumstances and is both initiated and controlled by the prefrontal cortex of the brain (or PFC). The emotional component (desire) is secondary in this case.

The situation in man is more complex than for instance in the cat [22] or the rat [21] on account of mankind's far greater linguistic skill. In man all sensory information can be replaced by language symbols and aggression can be expressed entirely in a linguistic way. Because of this, and because of the wider development of the prefrontal brain, the instructiveness of the cognitive control is greater. In this explanatory model the inhibition of the emotional response and the promotion of the cognitive response are functions of a certain area of the brain, the medial prefrontal cortex [23]. To put it simply: various parts of the brain affect each other's functioning [24].

The complex serotonerg system affects these structures. There are connections from the brain stem to all of the brain structures that were mentioned before. And, in order to achieve its effects, no fewer than 14 different types of receptors [25] are used, four of which are associated with the regulation of aggression. When the system is repeatedly over-stimulated, the receptors' sensitivity adapt and change what happens as a result. It is supposed that SSRIs stimulate aggression by inhibiting and

stimulating various brain structures, with three different types of responses occurring simultaneously: dysphoria (feelings of unease), the facilitation of the hot (emotional) aggression response and the facilitation of the cold (cognitive, instrumental) aggression response.

To sum up, there are indications that SSRIs may have a causal relationship with aggressive violent behavior, namely, by reducing inhibitions in a depression, by side effects such as akathisia and depersonalization, and by inhibiting as well as stimulating certain areas of the brain, thus promoting the emotional and the cognitive aggression response.

#### 4. Discussion

## 4.1 The importance of the concentration of paroxetine

According to the court's verdict in 2008, the locum had once again prescribed paroxetine to the woman, in a dose of 20 milligrams (1 tablet) once daily, but she did not fill the prescription. This was confirmed by the fact that the prescription was recovered in the woman's home, and also by the pharmacy's records, which showed that no medication had been delivered to the woman between 17 December 2007 and 3 September 2008.

In the consultation with her own GP on 3 September 2008 the dose was augmented because the GP had supposed that the 20 milligrams per day had not been effective. Had the woman started her medication on 6 August 2008, she would have been taking one tablet of the drug daily for 4 weeks, and there would not have been any improvement after 4 weeks' medication. (According to the standard GP guideline (Dutch General Practitioner Association, depressive disorder, M44, 2003), when insufficiently effective, the dose should be doubled after four to six weeks).

The woman later testified that she had taken three tablets of paroxetine on 3 September and two more on 4 September.

The toxicological analysis by the Dutch Forensic

Institute (NFI) showed traces of paroxetine in her blood and concluded that the concentration was so low that it could not have influenced her behavior. But later, during the trial, pharmacological experts agreed that the conclusion was wrong in several respects. On the basis of one single measurement of whole blood, taken quite some time after the drug has been ingested, it cannot be determined how high the concentration was shortly after taking the drug. Furthermore, in the use of serotonin reuptake inhibitors (occasional) cases are known where normal short-term use was followed by an outburst of violence.

If violence, as a side effect of an SSRI, is linked to the presence in the blood of a relevant quantity of the serotonin reuptake inhibitor [26] then the woman's violent behavior could be explained by the use of the drug. It should be added that only in those cases when at the time of the actions the accused lacked any insight into the scope of her actions, and their possible consequences, such a situation could lead to acquittal because intent is lacking. Such cases are rare because evil intent cannot be proven as in conditional intent cases. It must be evident that she did not know and could not know that such consequences might result after taking the drug. However, usually an accused has some insight in the scope of his actions, and legal practice shows that in such cases a (lack of) intent defense is often unsuccessful.

Sometimes the intent defense is unsuccessful, because an accused's "own culpability" is taken as the starting point in law. Intent is then assumed on the basis of *culpa in causa*. "Own culpability" might be assumed if it is determined that the accused has taken more medication than was prescribed, and that he also is aware, or can be aware, that a higher dose might lead to committing violence.

If, in the case being discussed, the woman took three tablets on her own accord, because she thought that 'there was no harm in that' and also that she has not heard or read anywhere that there could be harm in doing so, "own culpability" is out of the question. But if the woman knew about or was aware of this side effect, that is, that violent behavior may occur, then ingesting the (3 tablet) dose can be seen as "own culpability", and intent can be assumed. The discussion during the trial would then probably be whether or not the side effect is a rare one. If the side effect hardly ever occurs with users of the drug, it is reasonable for the defense to plead that "own culpability" is out of the question. When the concentration in the blood is of no importance and the woman never had a similar reaction in previous treatments, taking three tablets instead of the prescribed two cannot be held against her in relation to the violence against her daughter and her husband [27]. Finally, whether the woman's previous sub-arachnoid haemorrhage made her susceptible to an undesired effect of paroxetine is also questionable, but in other cases of violence and the use of serotonin reuptake inhibitors no descriptions of a similar affliction were found.

## 4.2 The Importance of a Delusion.

In this case the violence was disproportionate and of an instrumental nature, in which the actions were prepared over a period of several hours. This could be explained by a state of delusion in which reality is distorted. It is well known that in a paranoid delusional state a situation is perceived as threatening or dangerous when in reality there is no threat or danger. The woman's decision to commit suicide and to resort to violence towards her husband and daughter was perhaps impulsively colored after the argument with her daughter. It is known that negative aspects receive more attention during a depression, and in this the negative aspects may have case, overemphasized in the argument between mother and daughter, causing the woman's judgment to be ultimately impaired. But once her decision was made obviously there was nothing that could make her stop.

No fewer than seven experts were heard (four

behavioral experts, one behavioral toxicologist, one pharmacist and one pharmacologist) and various possible diagnoses were dealt with in the reports and during the trial: delusion, psychosis, delirium, depression, recurrent depression, intoxication, personality disorder, depersonalization, restricted awareness, lowering of barriers, paradoxical reaction, triggering effect, fear, primitive defense and coping mechanism, suicidality, tunnel vision, subarachnoid hemorrhage, organic brain disease, psycho-toxic effect. With so many differing expert opinions, it is difficult for the court to find its way through this maze, making this review appropriate. Because this case concerned a well-considered instrumental form of violence, psychopathological conditions that are associated with this kind of violence as psychosis (delusion) or depersonalization enter the picture. In depersonalization, feeling is divorced from cognition and apparently businesslike actions are possible [28]. Reasons for the occurrence of depersonalization are severe stress on account of the argument with her daughter, sleep deprivation because of staying up into the small hours, and the use of the SSRI.

The accused's conviction to kill herself as well as her daughter and husband may be qualified as a psychotic condition within the definition of Van der Waard [29]: a delusion could best be described as a shuttered unfalsifiable conviction with which the patient feels emotionally related and which is deemed implausible by most others because of the unshakeable certainty with which it is expressed. In the trial the woman testified that she had repeatedly struck first her husband and then her daughter forcefully in the head with an axe in the early hours of the morning, and that this was the only way for her to do any justice to herself and her family members. The verdict does not refer to the concussion she suffered as a result of running into the tree, and she could obviously remember everything quite well.

There can be no question of intent, if a person lacks any insight in the scope of the actions and their possible consequences, as is the case with when someone acts in a state of delusion. The woman's attorney maintained that she could not freely exercise her will and that she had been deprived of any insight in the scope of her actions and their possible consequences because her mental condition at the time of her deed was seriously impaired. According to the court, however, the experts did not agree on the existence of a delusion, psychosis, delirium or similar condition. They did agree, though, on a recurring depression, but not that it was a psychotic depression. The experts did not answer the question whether paroxetine can cause a delusion or whether during a delusion the use of paroxetine can produce or promote violent behavior.

#### 4.3 The affliction, the drug and the deed

Separate from the framework, from which the various parties to court proceedings approach the offence (see the Introduction, above), whether the affliction, or the drug, or both play a part should be addressed. As such, it should be determined whether an accused's actions take place under the influence of paroxetine because it can change certain psychological processes. The use of paroxetine may affect neurophysiologic functions and normal thought patterns. Accordingly, in the case being reviewed the woman's thoughts, that she did 'not want to inflict the grief of her suicide on her husband and daughter and that she had to take them along', could not be tested against the social norm: it is not acceptable to kill a fellow human being. The woman herself testified that she took paroxetine in the days preceding her act, and indeed, a low concentration of the drug was found in her blood. Even with low concentrations of paroxetine (or other serotonin reuptake inhibitors) there are cases in which (short term) use was followed by violence and suicide during the first week of the treatment. See, for instance, the case of Joseph Wesbecker, who, in the morning of 14 September 1989 in Kentucky, USA, shot twelve people while using a serotonin reuptake

inhibitor.

In the case being discussed, the woman had both the time and the opportunity to reflect on and to account for the consequences of her intended actions. It is remarkable that, in the period she was preparing her actions, the horrible nature of her intentions did not make her change her mind. Apparently she was convinced that her actions would spare more grief. The question is whether she did not register the appalling nature of her intended actions as such because of the paroxetine affected certain areas of the brain that typically have a corrective effect on such violent thoughts.

There are indications that **SSRIs** affect neurocognitive processes. For instance, Almeide and his colleagues [30], found that citalogram (a serotonin reuptake inhibitor) had a negative effect with healthy men on "contextual processing" tasks. The result was a temporary anomaly in being able to discriminate between new and familiar objects within 24 h after taking an anti-depressant. Similarly Harmer and her colleagues [31] found that healthy volunteers, with no history of depression, showed a diminished response in certain areas of the brain to pictures displaying a threat. What made this research special was that the time in which the picture was displayed was so short that the testee was not aware of the threatening content, and that, nevertheless, after the use of citalogram the areas of the brain in question responded less fiercely than without the use of citalogram. With people with a depression and a single dose of citalopram, the pictures with scary portrayals were perceived less fiercely [32].

To sum up, in certain persons with a depression, in the first few days of their treatment with an SSRI neurocognitive processes may be affected in such a way that feedback of intended behavior is diminished, the SSRI quite possibly has a contributory effect.

## 4.4 Assessing causality

Another question to consider is whether the

different players' frameworks with which they approach the legal proceedings could lead to a different result? For example, the accused's lawyer looks at the accused's action(s) as his starting point. In the case being reviewed, the woman's attorney argued that in view of her mental condition the woman should be found completely unaccountable and that her condition did not fit an assumption of premeditation. The court rejected this argument in its deliberations because, even if her action(s) were not to be attributed to her at all, this does not automatically lead to the conclusion that she was unable to act with premeditation or that the violent actions were not the result of an immediate impulse that caused her to act without delay. The circumstances outlined by the court showed that the accused had the time and the opportunity to consider and to account for the consequences of her intended actions. The question, though, is whether all of this happened while the woman was experiencing a pathological condition?

In court proceedings, the behavioral expert takes the disorder as his starting point. In this case the violence is instrumental, and accordingly, syndromes that may explain instrumental violence must be demonstrated or excluded. Earlier akathisia, depersonalization and delusion were mentioned, but depression is also of importance as SSRIs may have a causal relationship.

The effects of SSRIs have been mentioned by experts, such as a boosting effect or a barrier- (or inhibition-) lowering effect, but these were not considered to be likely explanations for a violent effect of the kind such as was perpetrated by the woman.

Depending on the experts' advice to the court, a wide range of possibilities may be presented, which only enter the picture when a disorder is suspected and when that disorder is linked to the facts of the accused's charge.

When paroxetine has an unknown, recorded, direct effect (manifesting in distortions of perception, cognitive distortions, depersonalization, akathisia), but is not dose-dependent, the woman could have been acquitted because intent is lacking. But if the effect was turned out to be dose-dependent and she was aware or could have been aware of such effects, culpability, or *culpa in causa*, enters the picture: it may be an unintended or unpursued effect, but nevertheless it is the result of taking more than prescribed.

If, as an element of the disorder, a (temporary) delusion exists caused by the SSRI medication, then complete unaccountability can be put forward, resulting in no criminal disposition. If that is not the case, and only the depression contributes to the action, the woman could be held only partly accountable. Should the chance of re-offending be deemed small, detention in a mental hospital remains, as typical punishment. A treatment order alone could still be a possibility because the court might decide to impose a conditional sentence, with the specific stipulation that the accused undergo treatment. The woman's preparedness to undergo treatment could be discussed in the court. Perhaps, in complex cases such as this, it is advisable for the public prosecutor and the defense attorney to avail themselves of the opportunity (since the introduction of the Act Experts in Criminal Cases) to have pre-trial deliberations with the magistrate about which additional questions regarding what content should be provided with in the report pro justice.

## 5. Conclusions

It is extremely difficult to find actual cases in which a person, by taking a drug prescribed by his doctor, acts in a (lethal) violent manner. When answering the question in this case as to whether that possibly exempted the woman from guilt, the court concluded that her accountability was lessened to a certain extent, in agreement with the experts' conclusions. However, the court also found that it had not been determined which element was exactly responsible for this, and to what extent, and that no circumstance had

been deemed likely to exclude culpability completely.

This verdict is acceptable to the authors, because no single factor is monocausally related to the offence. However, in their opinion, greater value should be attached to a contributory psycho-toxic effect from the use of medication (SSRIs) and to the disordered judgment and critical thinking that go along with the resulting (temporarily) psychopathological condition. Finally, the various parties to the proceedings should be aware of, and should keep in mind the different notional frameworks they use during criminal trials.

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#### References

- [1] T.I. Oei, (On) toerekenings vatbaarheid en het forensische betrekkings systeem, [(Un) accountability and the forensic relationships framework], Proces 75 (6) (1996) 133-137. (in Dutch with English abstract)
- [2] R.C. Brouwers, M. Drost, T.I. Oei, Medicatie en crimineel gedrag, (Medication and Criminal behaviour) in: L. de Vos, K. Venselaar, G. Timmermans (Eds.), Medicatie en Gedrag, Swets & Zeitlinger, Lisse, the Netherlands, 1998, pp. 159-173. (in Dutch)
- [3] R.H.B. Meyboom, Y.A. Hekster, C.G. Egberts, F.W.J. Gribnau, I.R. Edwards, Causal or Casual? The role of causality in pharmacovigilance, Drug Safety 17 (1997) 374-389.
- [4] U. Hegerl, Antidepressiva und suizidalität: nutzen-risiko-abschätzung, Der Nervenarzt 78 (2007)
   7-14. (in German with English abstract)
- [5] R.R. Reeves, M.E. Ladner, Antidepressant-induced suicidality: an update, CNS Neuroscience and Therapeutics16 (2010) 227-234.
- [6] H. Tandt, K. Audenaert, C. Van Heeringen, SSRI's en suicidaliteit bij volwassenen, adolescenten en kinderen (SSRIs and suicidality in adults, adoloescents and children), Tijdschrift voor Psychiatrie 51 (2009) 387-393. (in Dutch with English abstract)
- [7] D. Healy, A. Herxheimer, D.B. Menkes, Antidepressants

- and violence: problems at the interface of medicine and law, PLoS Med. 3 (9) (2006) 372.
- [8] www.ssristories.org/?s=aggression
- [9] SSRI's and Aggression. [Online], 208, 2009, p. 1-5, http://www.lareb.nl/Signalen/kwb 2009 3 ssris.
- [10] European Medicine Agency, Eudravigilance, Pharmacovigilance in the European economic area, 2013, available at http://eudravigilance.ema.europa.eu.
- [11] M.T. Walsh, T.G. Dinan, Selective serotonin reuptake inhibitors and violence: a review of the available evidence, Acta Psychiatrica Scandinavica 104 (2001) 84-91.
- [12] H.J. Möller, D.S. Baldwin, G. Goodwin, S. Kasper, A. Okasha, D.J. Stein, et al., Do SSRIs or antidepressants in general increase suicidality? WPA section on pharmacopsychiatry: consensus statement, European Archives of Psychiatry and Clinical Neuroscience 258 (supplement 3) (2008) 3-23.
- [13] H. Tandt, K. Audenaart, C. van Heeringen, SSRIs en suïcidaliteit bij volwassenen, adolocenten en kinderen, Tijdschrift voor Psychiatrie 51 (6) (2009) 387-393. (in Dutch with English abstract)
- [14] R.R. Reeves, M.E. Ladner, Antidepressant induced suicidality, an update, CNS Neuroscience and Therapeutics 16 (4) (2010) 227-234.
- [15] H.M. Van Praag, 5-HT-related, anxiety- and/or aggression-driven depression, International Clinical Psychopharmacology 9 (supplement 1) (1994) 5-6.
- [16] A.J.M. Loonen, S.M. Stahl, The mechanism of drug-induced akathisia, CNS Spectrums 15 (2010) 491-494.
- [17] L.P. Koliscak, E.H. Makela, Selective serotonin reuptake inhibitor-induced akathisia, Journal of the American Pharmacist Association 49 (2009) e28-e38.
- [18] R.M. Lane, SSRI-induced extrapyramidal side effects and akathisia: implications for treatment, Journal of Psychopharmacology 12 (1998) 192-214.
- [19] L. Hansen, A critical review of akathisia, and its possible association with suicidal behaviour, Human Psychopharmacologic Clinical Experiments 16 (2001) 495-505.
- [20] T.R. Gregg, A. Siegel, Brain structures and neurotransmitters regulating aggression in cats: implications for human aggression, Progression in Neuropsychopharmacological Biological Psychiatry 25 (2001) 91-140.
- [21] P.J. Mitchell, Antidepressant treatment and rodent aggressive behaviour, European Journal of Pharmacology 526 (2005) 147-162.
- [22] T.R. Gregg, A. Siegel, Brain structures and neurotransmitters regulating aggression in cats: implications for human aggression, Progress in

- Psychopharmacology and Biological Psychiatry 25 (1) (2001) 91-140.
- [23] F. Bruinsma, A.J.M. Loonen, Neurobiologie van cognitieve en emotionele motivatie, Neuropraxis 7 (2006) 77-86. (in Dutch)
- [24] J.W. Dalley, A.C. Mar, D. Economidou, T.W. Robbins, Neurobehavioral mechanisms of impulsity: fronto-striatal systems and functional neurochemistry, Pharmacological Biochemistry Behaviour 90 (2008) 250-60.
- [25] A.J.M. Loonen, The agile brain, The neurological backgrounds of the mental functions, Badhoevedorp, Mension, 2004, pp. 63-78.
- [26] A.G. Nielsen, R.S. Pedersen, L. Noehr-Jensen, P. Damkier, K. Brosen K, Two separate dose-dependent effects of paroxetine: mydriasis and inhibition of tramodol's O-demethylation via CYP2D6, European Journal of Clinical Pharmacology 66 (7) (2010) 655-660.
- [27] G B.F. Keulen, M. Otte, Opzet en Schuld (Intent and Guilt), Ars Aequi Libri, Nijmegen, 1999. (in Dutch)

- [28] M. Sierra, Depersonalization, a new look at a neglected syndrome, University Press, Cambridge, England, 2010.
- [29] R. van der Waard, Wat is een waan? Een fenomenologische beschouwing (What is a delusion? A phenomenological review), Tijdschrift voor Psychiatrie 48 (2006) 453-359. (in Dutch with English abstract)
- [30] S. Almeida, D.C. Glahn, S.V. Argyropoulos, S. Frangou, Acute citalopram administration may disrupt contextual information in healthy males, European Psychiatry 25 (2) (2010) 87-91.
- [31] C.J. Harmer, C.E. Mackay, C.B. Reid, P.J. Cowen, G.M. Goodwin, Antidepressant drug treatment modifies the neural processing of nonconscious threat cues, Biological Psychiatry 9 (2006) 816-820.
- [32] Z. Bhagwagar, P.J. Cowen, G.M. Goodwin, C.J. Harmer, Normalization of enhanced fear recognition by acute ssri treatment in subjects with a previous history of depression, American Journal of Psychiatry 161 (2004) 166-168.

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